A novel web-based public outreach tool for promoting the critical role of fundamental research in human health: Incorporating scrolling triggered video playback into the user experience

by
Tianxing Shi

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ABSTRACT

Fundamental research has played a significant role in human health and its impact continues to grow. As researchers probe deeper into cellular and molecular mechanisms of complex diseases like cancers, fundamental research has evolved into highly specialized subfields. These developments in research, however, have moved knowledge and understanding even further from the grasp of the general public. Meanwhile, not enough is done to effectively explain to the public why scientists do what they do. The subsequent communication breakdown between the science community and the public may cause decreased research funding, lack of interest in pursuing careers in science, and a growing ignorance on the part of the public regarding the value of fundamental science. This thesis seeks to bridge this communication gap by developing a public outreach program to clearly explain the principles of fundamental research and address its importance in improving human health.

This thesis explores the effectiveness of making a public outreach program engaging and effective by employing a combination of visual representations, including 3D models, animations, 2D motion graphics, user interface and experience designs. The final product will be presented on an interactive video website using a recently developed JavaScript coded technique called "Scrolling Triggered Video Playback". This technique allows viewers to play and playback the videos by scrolling up and down based on their reading pace. Content of the word story and art assets is based on research projects carried out in the lab of Douglas Robinson in the department of Cell Biology at Johns Hopkins University School of Medicine. The Robinson Lab studies cell mechanics, including mechanoresponsive behavior of cells, and applies the concepts they observe to developing novel therapeutics for complex diseases, including cancer and chronic obstructive pulmonary diseases (COPD).

Expected benefit of this public outreach program is to effectively communicate the value and importance of fundamental research to the public. The goal of the program is to assist viewers

in understanding the general concepts behind fundamental research by using current topics from the Robinson lab as examples, and in doing so cultivate an appreciation of the relevance of science to people's lives.

By Tianxing Mary Shi

Chairpersons of the Supervisory Committee

Douglas N. Robinson, Ph.D.
Professor, Departments of Cell Biology, Pharmacology and Molecular Sciences,
Chemical and Biomolecular Engineering, Johns Hopkins University School of Medicine

David A. Rini, MA, CMI, FAMI
Associate Professor, Department of Art as Applied to Medicine
Johns Hopkins University School of Medicine

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INTRODUCTION

Overview

Fundamental research, also called basic science research has played a significant role in human health and its impact continues to grow. During the 20th century, the average life expectancy in the United States rose from 47 years to more than 76 years (Science Policy, 2015). Much of this increase, particularly in recent decades, is the result of medical advances arising from fundamental research. Biomedical research, one of the major branches of fundamental research, has conquered many bacterial, viral, and parasitic diseases that have plagued humans for centuries. Polio, diphtheria, smallpox, and pneumonia are no longer necessarily fatal diseases (NIGMS, 2011). But still, humankind continues to be confronted by more complex diseases such as cancer, cardiovascular disease, chronic obstructive pulmonary disease, and diabetes. These diseases, once thought to be the "natural" consequences of aging, are now understood to be cumulative dysfunction of molecular mechanisms within cells and tissues, which may be preventable or curable if scientists understand their basic mechanisms and learn to intervene at the initial stages (NIGMS, 2011). As researchers probe deeper into these perplexing cellular and molecular mechanisms, fundamental research has evolved into more advanced and specialized subfields. These developments in scientific research, however, have moved knowledge and understanding even further from the grasp of the general public (Short, 2013). Meanwhile, not enough is done to effectively explain to the public why scientists do what they do. The subsequent communication breakdown between the science community and the public may cause a decrease in research funding, lack of interest in pursuing careers in science, and a growing ignorance on the part of the public regarding the value and importance of fundamental science (Pham, 2016).

Hence, there is a significant and growing need to bridge the communication gap between researchers and the public, including policy makers and funders. Because the majority of

the general public does not closely follow scientific developments beyond what is taught in secondary education (Short, 2013), it is the responsibility of scientists and scientific communicators to convey the information in an appropriate way to help people understand the general concepts behind current research, as well as to cultivate an appreciation of the relevance of science to people's lives.

This thesis project explores the effectiveness of employing a combination of visual elements in order to make a public outreach program engaging and effective. The process must begin by first understanding the public's comprehension and attitudes towards fundamental research, as well as the specific challenges of communicating fundamental science, examined in the following section.

Public's Comprehension and Attitudes Towards Fundamental Research

Knowledge levels among the general public, if measured as simple recall of scientific facts, have remained fairly high over time (Scheufele, 2013). However, according to National Science Board (2016), only one in four Americans (26 percent) could explain "what it means to study something scientifically," and only half of Americans (53 percent) had a correct understanding of randomized controlled experiments. These findings demonstrate that knowledge of the scientific process and methods appears to not be widespread.

There are also alarming deficits in the public's understanding of science in general, highlighted in a recent study by the Wellcome Trust (2016), which found that only 9% of respondents were aware of the meaning of antibiotic resistance; 31% believed that it is their own bodies that have become resistant to antibiotics. Similar levels of ignorance prevail regarding the fact that antibiotics kill only bacteria and not viruses, and are therefore not suitable for treating flu or the common cold. Another recent survey published by The Pew Research Group and the American Association for the Advancement of Science also highlighted the obvious differences between scientists and the general public when asked for their opinions on various relevant topics such

as whether humans have evolved over time, whether genetically modified foods are safe to eat, and whether climate change is because of human activity (Pham, 2016).

In addition, few people outside the scientific community consume scientific information regularly (Boczkowski and Mitchelstein, 2013), although they encounter and benefit from science often in their everyday lives. Many people profess interest in science news, yet only 16 percent of the public say that they follow news about science and technology "very closely" (Mitchell et al., 2016). This percentage has remained below 18 percent since 2000 (National Science Board, 2014). Other statistics also support this finding. According to the General Social Survey (GSS 2008), 86% of respondents expressed interest in new scientific discoveries. However, this interest is generally passive in nature. For example, only 13% of the 2008 GSS respondents say that they follow science and technology news closely and only half had visited a zoo, aquarium, or science-related museum within the past year.

This conflict between expressed interest and active interest in science also manifests itself in American public opinion on the federal funding of basic science research. According to General Social Survey (GSS, 2006), 90% of respondents agree that "science research is necessary and should be supported by the federal government". However, the importance of federal funding for science relative to that of other areas is more controversial, with the majority of the Americans believing that federal investment in areas such as economic growth is more important than investment in research and discovery. These findings suggest that compared to other causes that affect society, basic science research is a relatively low priority for the public. Furthermore, the essential role of research and discovery in facilitating the exact economic growth that the public seeks, is often neglected.

The general lack of effective communication between the science community and the general public is responsible, in part, for the lack of support for fundamental research. This situation can be and should be improved. The solution should begin with understanding the factors that make scientific communication difficult.

The Complexities of Communicating Science

Science communication is more complex than simply translating the jargon of science into plain language. The complexity stems from the natural sophistication of fundamental science and a lack of understanding and interaction between science community and the public (Leonard, 2010).

The nature of the scientific information itself can pose a challenge for communication. First, the topics and subject matter studied by researchers are abstract and often unfamiliar to the lay public, for example, cell mechanics and the amoeba cell model. Much of the subject matter being studied currently is at the micro-level, which can be observed only with a microscope and other high-performance lab equipment. Even though many microscopic images are available online, not being able to see the subject matter in person, may prevent the public from becoming fully engaged and understanding the impact the topics have on everyday life. Second, the extensive science vocabulary used by scientists in academic publications adds to the confusion. The terminology, while accurate and concise, often makes the information more daunting than enticing and proves to be an additional hurdle for people outside of science to understand. Complex scientific language, therefore, shows limited benefit in public outreach. Third, numerical information and concepts referred to as "numeracy" are often an important part of scientific methods. However, the public often finds mathematic concepts and tools such as formula, function and statistical tests, confusing and abstract. Many people, without specialized knowledge of these concepts, have difficulty understanding quantitative and probabilistic information. Challenges of numeracy oftentimes even impact scientists outside of their areas of expertise.

Additionally, scientific uncertainty provides another barrier for communication. Scientific research is expected to yield rule-governed methods for producing reliable information that is useful to society, through a long-term cumulative process. However, scientific findings often

represent work in progress without a solid conclusion. These findings maybe applicable in particular contexts or populations, or are inconclusive on topics for which the public would prefer a clear, definitive answer (Fischhoff, 2013).

There are not sufficient effective visual representations available to the public to help reduce the communication barrier.

Figures and graphs are often included in scientific papers for researchers to achieve better communication amongst themselves. These visual elements are not designed for and therefore remain abstract to the public. Extra effort needs to be made by scientific communicators to interpret these figures and graphs with simplified graphic patterns, effective colors, careful wording and design elements to facilitate the communication to a lay audience.

Moreover, the media tends to oversimplify science, with inadequate differentiation between well-founded and poorly supported scientific concepts (Pham, 2016). For example, science news on transgenic food safety and vaccines are often seen in newspapers and on TV programs. Such information may shape people's every day decision making. Yet many of the sources of the information are invalid. Over time, miscommunication and even mistrust between the research community and the general public can be further accumulated.

Understanding Basic Science and Basic Science Research

Basic science principally refers to the knowledge and discoveries that lead to a better understanding of living and non-living things in our environment, including ourselves. Physics, Chemistry, Mathematics and Biology fall under this basic science umbrella. Over time, various interdisciplinary branches have been developed from these disciplines. For example, the study of biology has evolved into computational biology, biophysics and biochemistry, all of which involve aspects not only of biology but also math, physics, chemistry and even computer science.

Fundamental research focuses on using knowledge of basic science to understand the mechanisms behind sophisticated phenomena, such as human body in illness. By generating hypothesis, observing, testing, measuring, analyzing and replicating, fundamental research has provided and continues to offer an understanding and foundation for the production of new technologies, including novel therapies for the treatment of complex diseases.

Fundamental research is essentially a question driven process. Researchers are generally driven by three basic questions. (1) How do things function normally? For example, the human body at different levels of organization, from the organ system to organs, tissues, cells and molecules. (2) What happens when the system breaks? For instance, a certain disease may develop due to a disrupted signaling transduction pathway and subsequent altered gene expression. (3) How to fix it? The answer to this requires understanding of: how diseased tissue is formed and developed; how cell behaves and responds to its changing microenvironment that causes disease; how modified protein disrupts cellular function; how mutated gene alters subsequent protein expression.

Finding the answers to these basic questions is greatly hindered by the extreme complexity of the science and sheer numbers of molecules and cells involved in the human system. Scientists, therefore, have developed a series of strategies and methods to cope with this challenge.

Understanding Research Strategies

The strategies outlined in this section are based on research projects carried out in the lab of Douglas Robinson in the Department of Cell Biology at Johns Hopkins University School of Medicine. The Robinson Lab studies cell mechanics, including mechano-responsive behavior of cells, and applies the concepts they are learning to developing novel therapeutics for complex diseases, such as cancer and chronic obstructive pulmonary diseases (COPD).

Research Background

Pancreatic cancer has been a popular target of biomedical research because it represents one of the leading causes of cancer related death despite advances in medical therapy and surgical techniques. Pancreatic cancer is hard to treat, largely because patients are non-symptomatic until the disease has progressed to the late-stage metastatic state.

Cancer metastasis is the process in which cancer cells break away from where they are initially formed (primary tumor), travel through blood vessels or the lymphatic system, and form new tumors in other parts of the body. These migrating cells are referred to as metastatic cancer cells and generally are characterized by altered cell mechanics, such as decreases in cell stiffness and cortical tension by up to 70% (Surcel et al. PNAS 2015.), which leads to increased deformability. In addition, these alterations in deformability are frequently associated with changes in the manner in which cancer cells sense and interpret mechanical inputs (forces and stresses, and stiffness of surrounding matrix).

For invasive pancreatic cancer, the cancer cells are much more deformable than normal pancreatic ductal epithelial cells and are correspondingly more mechanosensitive. It is rational then to hypothesize that metastasis is potentially related to altered cell mechanics including deformability and mechanosensitivity.

Hence, scientists from Robinson Lab have developed a workflow from fundamental studies in the model systems to therapeutic targets in the human system (Luo et al. Nat. Mater. 2013; Mohan et al. Interface 2015; Schiffhauer et al. Curr. Biol. 2016; Surcel et al. PNAS 2015), to uncover the cellular and molecular components involved in the process of cell shape change. The workflow (**Fig. 1**) is generalized into a series of four strategies that are included in the thesis: Simplify (Model system), Predict (Computational modeling), Test (Human system) and Screen (High-throughput chemical screening).

Figure 1. A workflow from fundamentals to therapeutic targets. The workflow is generalized into a series of four methods: Simplify (Model system), Predict (Computational modeling), Test (Human system) and Screen (High-throughput chemical screening). Text included in the image is not intended to be read.

(1) **Simplify: Model system**

Human beings are very complex multicellular organisms. But our cells contain the same fundamental materials as those of all living organisms. Researchers, therefore, can learn an abundance of knowledge about how our bodies work by studying simpler organisms, often called model organisms, in the lab setting.

In these model organisms, experiments can be designed and carried out to define fundamental principles of biology and disease. Common features of model organisms include rapid growth to high cell densities in an inexpensive medium, as well as accessible means of observation and manipulation. Classic model organisms range from single-celled bacteria to more complex animals such as mice. For example, the bacteria *Escherichia coli* (E. coli) is an excellent tool for genetic engineering and synthetic biology; fruit flies and honeybees are important model organisms for learning about how genes and the environment interact to affect behavior; worms and zebrafish can regrow missing or injured body parts, thus are used to learn about how cells and tissues regenerate. Mice are commonly used to study disease development and test novel therapies including drugs and vaccines (NIGMS, 2011).

Dictyostelium discoideum (a.k.a. Dicty) (**Fig. 2**), a type of amoebozoan is a relatively recent addition to the list of model organisms for fundamental research. Dicty has proven to be a very effective tool in studying human cell behaviors. Living most of its life as a single, free-living amoeba consuming bacteria, its flexible plasma membrane without a rigid cell wall permits it to be highly motile, similar to human leukocytes. When it runs out of food, these free-living cells

then join up and cooperate like an intelligent multicellular organism, forming many structures found in multicellular organisms such as epithelial tissues. Thus, these behaviors capture many of those presented by human cells and tissues. Moreover, the 34 Mb genome of Dicty contains many genes that are homologous to those in higher eukaryotes, including humans (DictyBase, 2010). These genes are either absent or are less accessible in other model organisms.

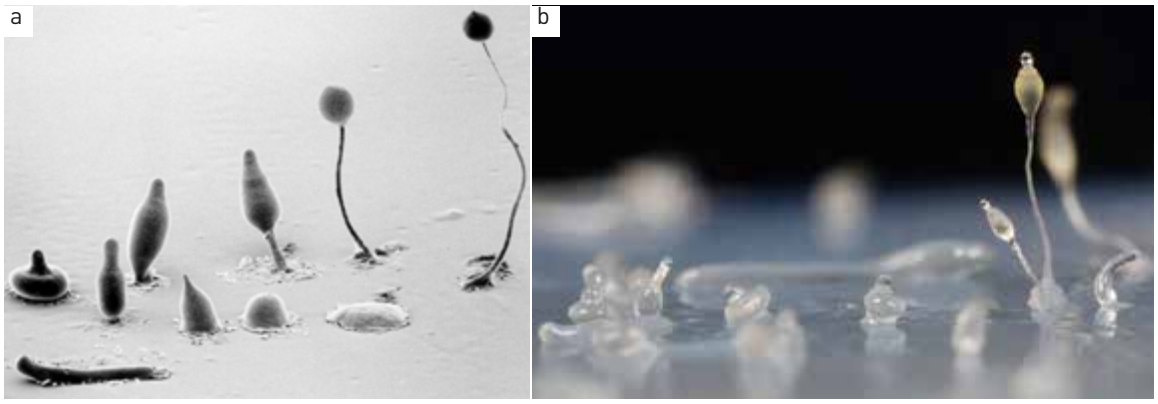

Figure 2a. SEM of *Dictyostelium discoideum* (Dicty) developmental stages. Copyright M.J. Grimson & R.L. Blanton; Biological Sciences Electron Microscopy Laboratory, Texas Tech University. **2b. The beauty of *Dictyostelium discoideum* under stereoscope.**

Many phases of health and disease depend on the behaviors of individual cells that are clearly displayed in Dicty. For example, cytokinesis, a process easily observed in Dicty, is critical in understanding cell proliferation and is therefore an integral part of immune response, tissue maintenance, and cancer development. Further, as a model shape change process, cytokinesis captures most of the critical features, including the biochemistry and mechanics of cell shape change events more broadly. Cell motility, a characteristic feature of Dicty, is an essential early event in the metastasis of tumor cells and in angiogenesis by endothelial cells. Chemotaxis and phagocytosis are prominent features of Dicty, which are powerful for studying mechanisms behind inflammation, asthma, immune surveillance and antigen presentation (DictyBase, 2010). More importantly, Dicty is uncomplicated to handle in lab settings. The size of Dicty is the same size as a human leukocyte and can be easily observed under light microscope. Fluorescence

labeling further enhances the presentation of its cellular components (**Fig. 3**), and Dicty are particularly amenable to genetic manipulation. Further, Dicty cells are easily studied biophysically. For mechanical studies, one common method is micropipette aspiration (MPA) (**Fig. 4**). In this technique, a small diameter glass pipette is brought into contact with the Dicty cell. A known suction pressure is then applied within the pipette, causing an aspiration of the cell into the pipette. By measuring the length of aspiration, several important cell mechanical properties, such as cortical tension, can be calculated. Cell deformability, in turn, could be analyzed. The combination of fluorescence microscopy and micropipette aspiration (**Fig. 5**) enables high quality visualization of molecular components, including various proteins, during the process of cell shape change, as presented in the study of cell shape control at the Robinson Lab. Their studies in Dicty cells have revealed several fundamental concepts:

(1) Cell shape is maintained by a dynamic network of specific cytoskeletal proteins that interact tightly with the cell membrane.

(2) Within this network, a specific subset of cytoskeletal proteins sense and respond to mechanical stimuli and trigger subsequent cell shape change. This property is called mechanoresponsiveness, and these proteins are often referred to mechanoresponsive or mechanosensitive. These proteins are also critical components in cell movement and deformation, and are coordinated through a mechanical and biochemical feedback system.

(3) If the expression of these proteins becomes abnormal, generally elevated, this leads to disrupted cell shape changes, movement, and mechanoresponsive. In cancer, this imbalance at protein level and migration at cell level could mutually reinforce each other to aggravate cancer metastasis.

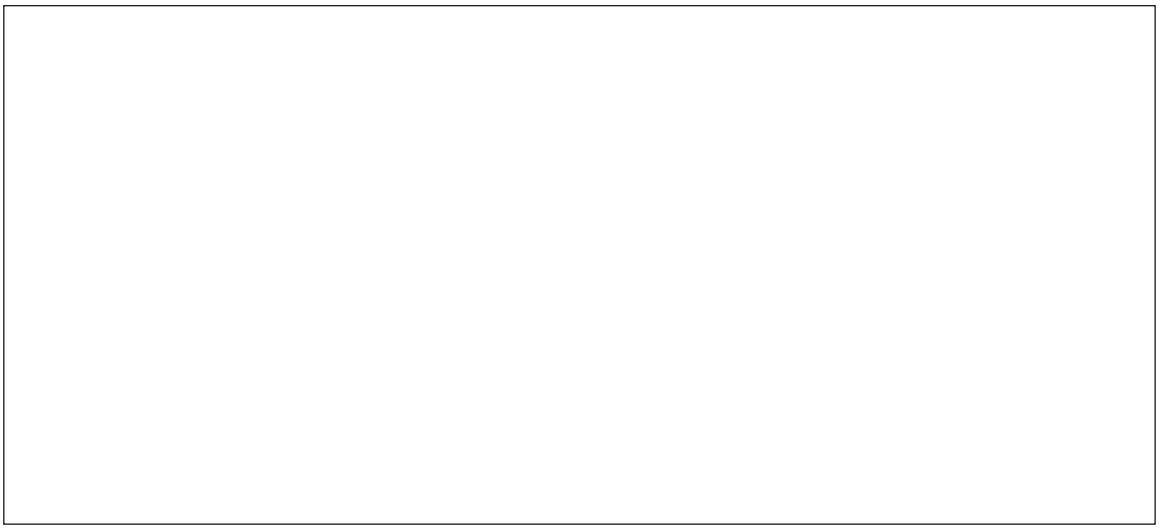

Figure 3. Fluorescence labeling showing the distribution of cytoskeletal proteins in different mutants of Dictyostelium under confocal microscopy (Luo et al. 2013).

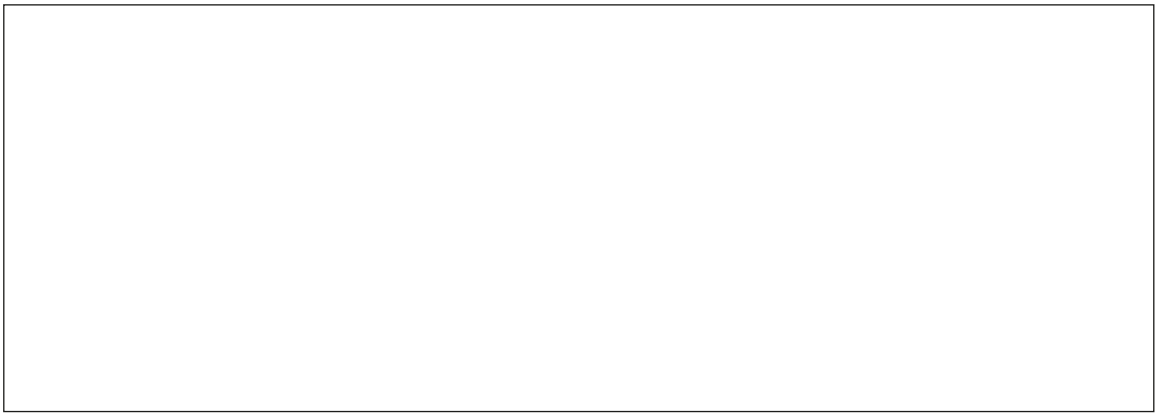

Figure 4. Manipulation of cells by Micropipette Aspiration for cortical tension and mechanosensitivity analysis (Kee and Robinson. 2013). Text not intended to be read.

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Figure 5.Manipulation of Dicty cells by fluorescence labelling and micropipette aspiration for studying cell shape control (Effler et al. 2006; Ren et al. 2009; Kee et al. 2012).

(2) Predict: Computational modeling

Because of the considerable amount of sister proteins (or paralogs - proteins share the same origin) in human system that do not exist in Dicty cells (the Dicty genome is more streamlined), and due to the wide range of proteins in general, experimental results from these model organisms are still inconclusive in identifying the proteins that plays the role in human health and diseases. Computational Modeling, therefore, helps bridge the gap.

Figure 6. Example of computational modeling. Digital imaging and kinetic simulations were included in the process (Luo et al. 2013). Text not intended to be read.

Myosins are a superfamily of motor proteins, well known for their roles in a wide range of cell motility processes. Studies in Dicty show that Myosin II is one of the mechanoresponsive proteins within the network of cytoskeleton, involved in cell shape maintenance and changes, as mentioned above. The three paralogs in human cells, namely Myosin IIA, IIB and IIC, were suspected to share the same property. Likewise, other mechanoresponsive proteins discovered in Dicty, such as alpha-actinin (ACTN) and Filamin, also have several sister proteins in human cells, which were also possibly to be utilized by cancer cells to achieve metastasis.

To analyze the similarity and differences between these sister proteins in human cells and the homologous protein in Dicty, computer models were developed and utilized. To develop the computer models, and the underlying physical theories, experimental datasets generated from comprehensive investigation of Dicty were collected and analyzed, during which digital imaging, math, physics, and computer science were involved (**Fig. 6)**. The theories allowed researchers to simulate the dynamics of sister proteins in the human system. The statistical results of these simulations helped researchers predict several protein attributes in human cells, such as mechanosensivity, reaction rate and localization patterns under different levels of mechanical stimulation. For instance, one of the simulation results (**Fig. 7**) suggested that under external mechanical stimulation, ACTN4 (one of the alpha-actinin paralogs) increased in intensity while

Figure 7. A force-dependent model based on Actin-binding affinity predicts the mechanoaccumulative behavior of α-Actinin sister proteins (Schiffhauer el al. 2016).

ACTN1 did not, indicating that ACTN4 but not ACTN1, was mechanoresponsive.

The predictive power of the computational models decreases the range of molecular components to be tested in human cells and tissues, as well as decreases the scope of the experimental design. These models, therefore, are very helpful tools in translating experimental results from model organisms to human systems. Moreover, computational modeling allows scientists to simulate variations rather efficiently, saving considerable time, money, and materials.

(3) Test in human system

With the guide of the computational predictions, experimental designs in human systems become straightforward. Human derived cells and tissues were utilized at this point to test if the simulation correctly predicted the cell and protein behaviors.

Human derived cells are cells taken from human bodies, isolated and cultured in the laboratory under specific nutrients and space. Although they are removed from their normal context in human tissues, they still provide an invaluable tool for deciphering human disease relevant biology. Isolated cells allow for the examination of stepwise alterations in the structural and genetic makeup of the cell under controlled environments. However, many of these controlled environmental conditions include scenarios that reconstitute conditions the cells experience in normal tissue context. This ability to reconstitute defined tissue contexts with well-defined cells is especially valuable for studying complex tissues such as the pancreas, which is composed of various cell types and where in vivo examination of individual cells would be difficult. Further, the reconstituted tissue-like environments also allow for the ability to probe the cells and tissues, for example for mechanical studies.

In the studies carried out in the Robinson Lab, several human-derived cells were investigated, to determine if the computational prediction of the mechanoresponsive property of the sister proteins in the human system is correct. These cell lines include immortalized Human Pancreatic Ductal Epithelial cells (HPDE), stage II pancreatic adenocarcinoma-derived cells

(Panc10.05), stage IV ascites-metastasis-derived cells (AsPC-1). HPDE cells are also used as a near normal pancreatic ductal epithelial cell comparator, while the others represent cancer cells in different disease states. In these cells, the targeted proteins were labeled with fluorescent proteins. Similar to the study of cell mechanics in Dicty, micropipette aspiration (MPA) was used to apply the external mechanical stimulation. The localization and concentration of the labelled proteins in response to applied external stress were observed and measured. The experimental results (**Fig. 8**) were consistent with computational simulations, which confirmed the mechanoresponsive property of several previously suspected proteins, including Myosin IIC and ACTN4. The results also reflected the active involvement of these proteins in the process of cell shape change in both normal and cancer cells. Furthermore, cancer cells displayed higher levels of cell deformation compared to the control group, as well as higher concentration of these proteins at the sites of deformation. This positive correlation between cell deformability and mechanoresponsive protein level in human derived cells highly suggested that mechanoresponsive proteins might be harnessed by cancer cells, leading to altered cell shape control and cell motility.

Figure 8. Representative images across multiple human derived cell lines show peak intensity after applied stress in MPA mechanoresponse experiments (Surcel el al, 2017).

This correlation between cell shape change and protein dynamics was then further tested in patients' tissue samples isolated directly during surgical resection to remove the patient's tumors (with patient consent). These samples provide direct information about disease states and are used to test whether discoveries in model organisms and human-derived cells are consistent with real-life situations.

To test if these mechanosensory proteins, such as Myosin IIC, were over produced in pancreatic cancer, tissue samples from PDAC patients were collected. Testing was achieved by using immunohistochemistry (antigen-antibody and tissue-based reaction), a method of tissue imaging. Secondary antibodies coupled with horse radish peroxidase (HRP) were applied to the tissue slides followed by the chromagen DAB with which the HRP reacts to create a brown color. Where the tissue turns brown reflects where the protein is found, and protein concentration is represented by the intensity of the pigments. The resulting images observed under light microscope indicate that Myosin IIC and other mechanosensory proteins were highly up-regulated in the pancreatic ductal adenocarcinoma of patients, compared to normal tissues (**Fig. 9**). The level of up-regulation is positively correlated to the stage of pancreatic cancer, further confirming that these mechanosensory proteins are critical components of cancer cell

Figure 9. The mechanoresponsive machinery is elevated in pancreatic ductal adenocarcinoma in human pancreatic tissue (Surcel el al, 2017).

shape change and migration. Hence, these proteins might be potential therapeutic targets in reducing cancer metastasis.

(4) Screening: High-throughput chemical screening system

The experimental results from both model and human systems suggest that one rational therapeutic approach is to correct tumor cell behavior by reducing cell deformation (in other word, increasing cell stiffness), which would in turn, reduce metastatic potential of cancer. This could be achieved by interfering with the mechanosensitive proteins like Myosin IIC, using small-modulators (small compounds).

To seek for effective small compounds, an in vivo, high-throughput, chemical screening system was developed. This system enables the efficient discovery of possible drug precursors. Large numbers of compounds from compound libraries were added to and interact with cells in thousands of reacting wells. Sensitive detectors and data processing software made it possible to accurately pick up these potential compounds based on their ability to inhibit cell shape change. A small compound, 4-hydroxyacetophenone (4-HAP) was characterized by the Robinson Lab. 4-HAP reduces cell deformation by forcing Myosin II to re-localize along the cell cortex. Such re-localization of mechanosensitive proteins increases cellular cortical tension and subsequent cell stiffness. In a mouse liver metastasis model, 4-HAP treatment (**Fig. 10**) reduced the metastasis of pancreatic tumors to liver, in comparison with the control (Surcel el al, 2017).

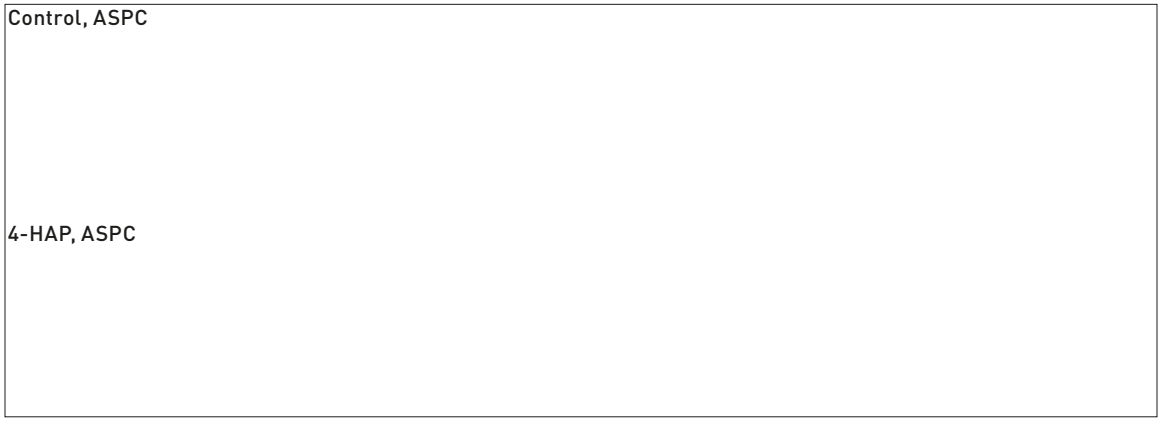


Figure 10. 4-HAP treatment in a murine model of metastatic pancreatic cancer (Surcel el al, 2017).

Objectives

This project explores the effectiveness of employing a combination of visual elements, including 3D models and animations, 2D motion graphics and interactive designs, for making an engaging and successful public outreach piece. The final product will be presented in the form of an interactive website, intended to provide a broad overview of fundamental research to the general public in an aesthetic and easy to navigate format.

The content will be divided into the following three sections:
(1) Landing Page – To draw attention and inspires further consideration.
(2) Introduction Page - To provide background information on fundamental research.
(3) Research Strategies – To explain why scientists do what they do in the context of the study of cell shape control in cancer treatment (specifically from the Robinson Lab at Johns Hopkins School of Medicine).

Audience

The primary audience will be composed of members of the lay public including potential funders and policy makers who may not have a science background. The appreciation of the importance and relevance of fundamental science is critical in gaining the appropriate support for biomedical research that leads to better healthcare. The secondary audiences are scientists and bio-communicators who are interested in public outreach about fundamental research.

MATERIALS AND METHODS

Literature Review

Literature and web reviews were initially conducted on the following topics:

(1) The current state of science outreach and policy.

Surveys and relative social studies were reviewed. Statistical information collected from various sources, including General Social Survey, Wellcome Trust, American Association for the Advancement of Science, and National Science Board, indicate the existence of a significant communication gap between the science community and the general public.

(2) Information regarding major fundamental research concepts.

Reading materials on general research concepts were retrieved from the websites of National Institute of Health, Nature, and several science blogs, such as, Science Policy and Johns Hopkins Health Review. Both the content and the language used in these articles were analyzed and served as examples in developing an appropriate and effective word story for this project.

(3) Particular examples of fundamental research including studies of cell cytokinesis and cellular mechanosensing.

Publications from the Robinson Lab were reviewed. The workflow of their research into cell shape control and mechanosensing were generalized into a series of four strategies. These research strategies serve as a storyline to walk the viewers through a research process for developing novel therapeutics, explaining why and how researchers do what they do.

Wireframe and Word Story Development

As information was collected during literature review, wireframe and word story for the website were developed. The wireframes were helpful in discussing both the content to be included in the program, and the flow of the design. During the initial stage, the wireframe

underwent a series of iterations (**Fig. 11**). The first few versions were hand-written flowcharts used during brainstorming sessions to efficiently exchange ideas. More detailed frames were then combined with text to more completely outline the story. User experience design was also incorporated into the later versions. After several rounds of discussion, three levels of information were identified for the final flowchart (**Fig 12**). The program begins with the question "How does fundamental research help you?" to build a connection with the audience and to

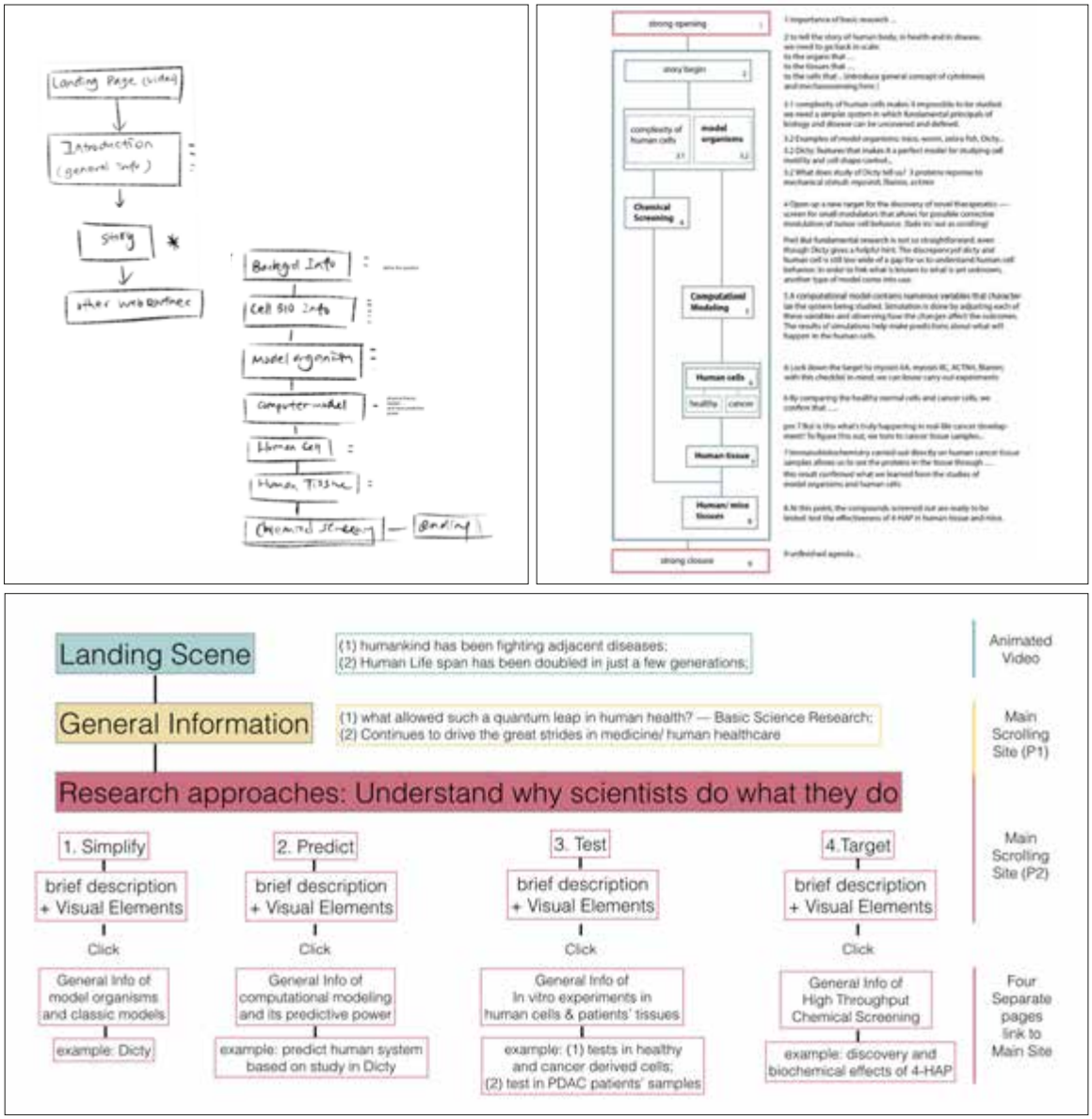


Figure 11. Flowcharts development. Not all text is intended to be read.

inspire thoughts. The second part of the project introduces several aspects of fundamental research ranging from basic information, such as how to more advanced concepts. Once the connection with the viewers is built, the definition and general process of doing research is introduced, followed by the complexity of studying the basic mechanisms of the human system, and corresponding strategies. The third section further explains the strategies. It is designed to increase in detail as the user progressed through the section, covering the general purpose of each strategy, the research approaches used to achieve each goal, and examples of specific studies from Robinson Lab that apply these approaches to investigate molecular and cellular processes of disease.

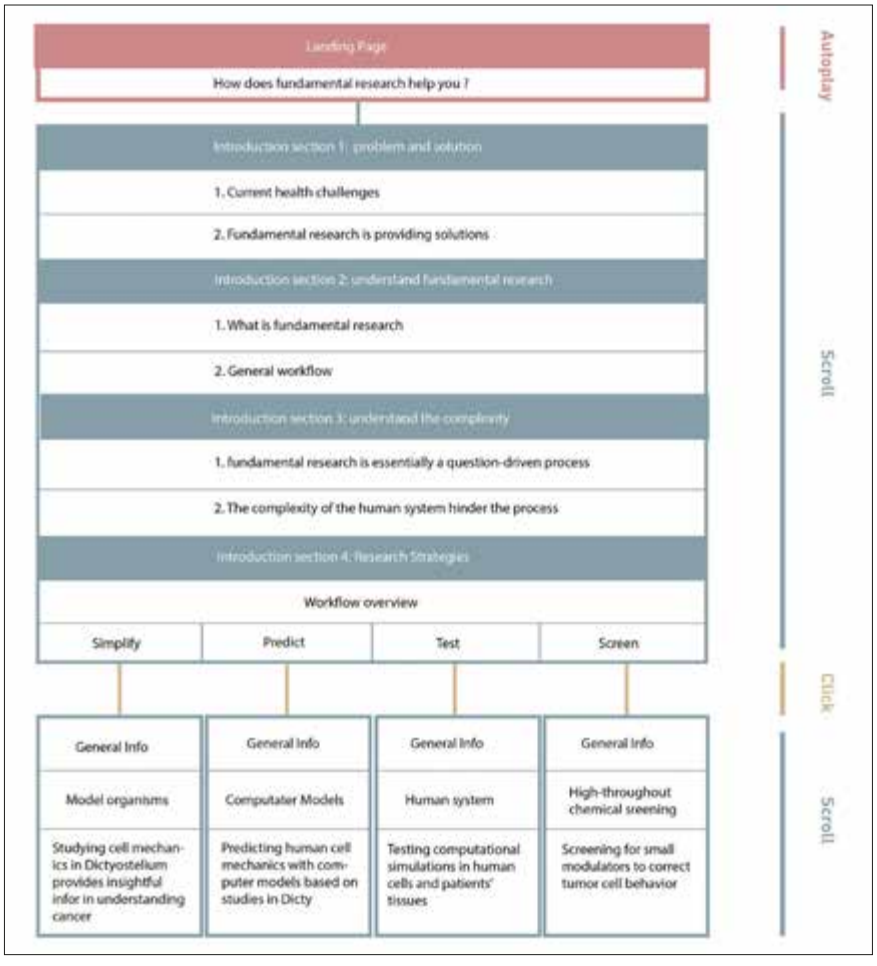


Figure 12. Finalized flowchart. Legible text in subsequent figures.

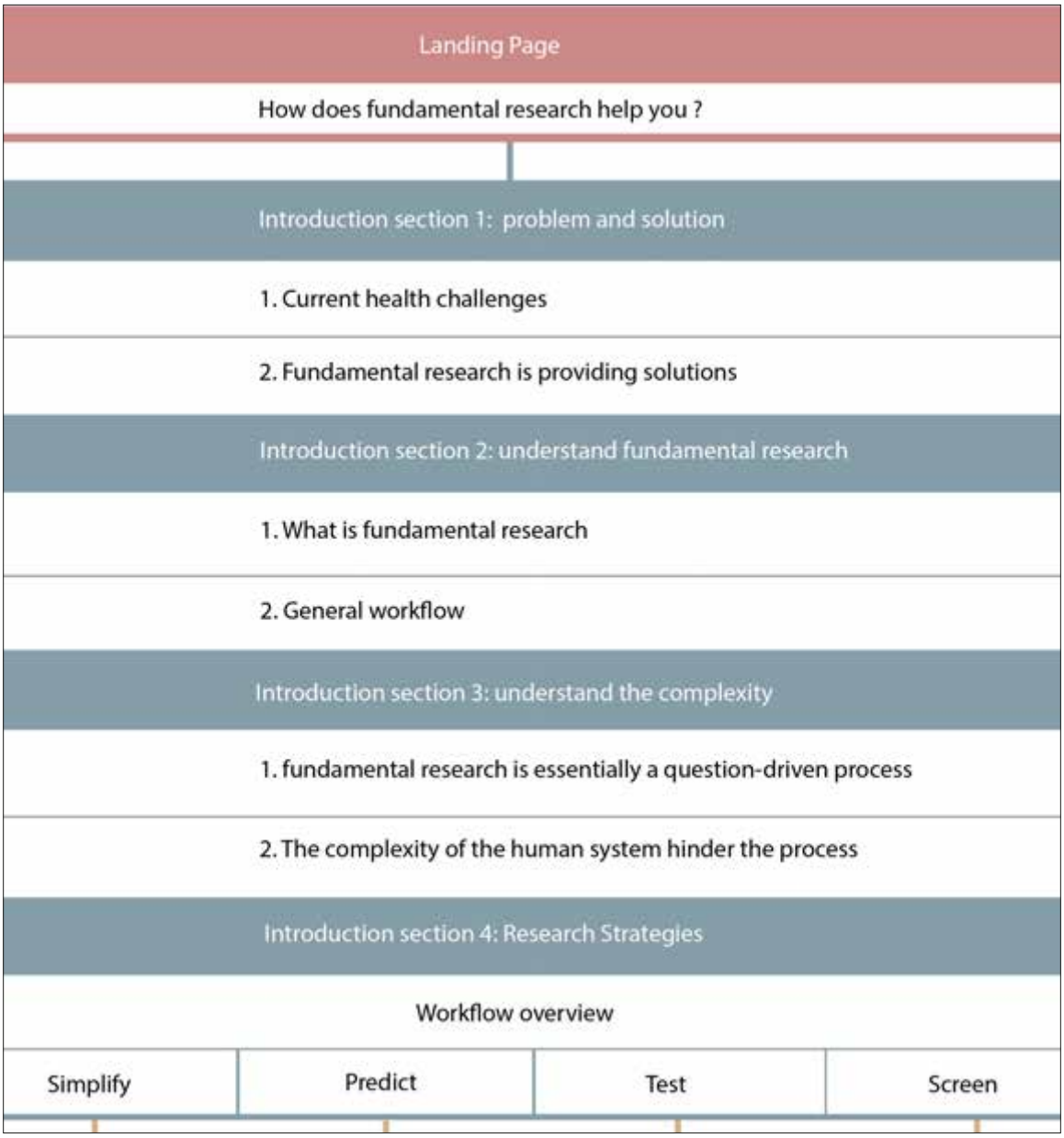


Figure 12a. Finalized flowchart part 1. Landing page and introduction sections.

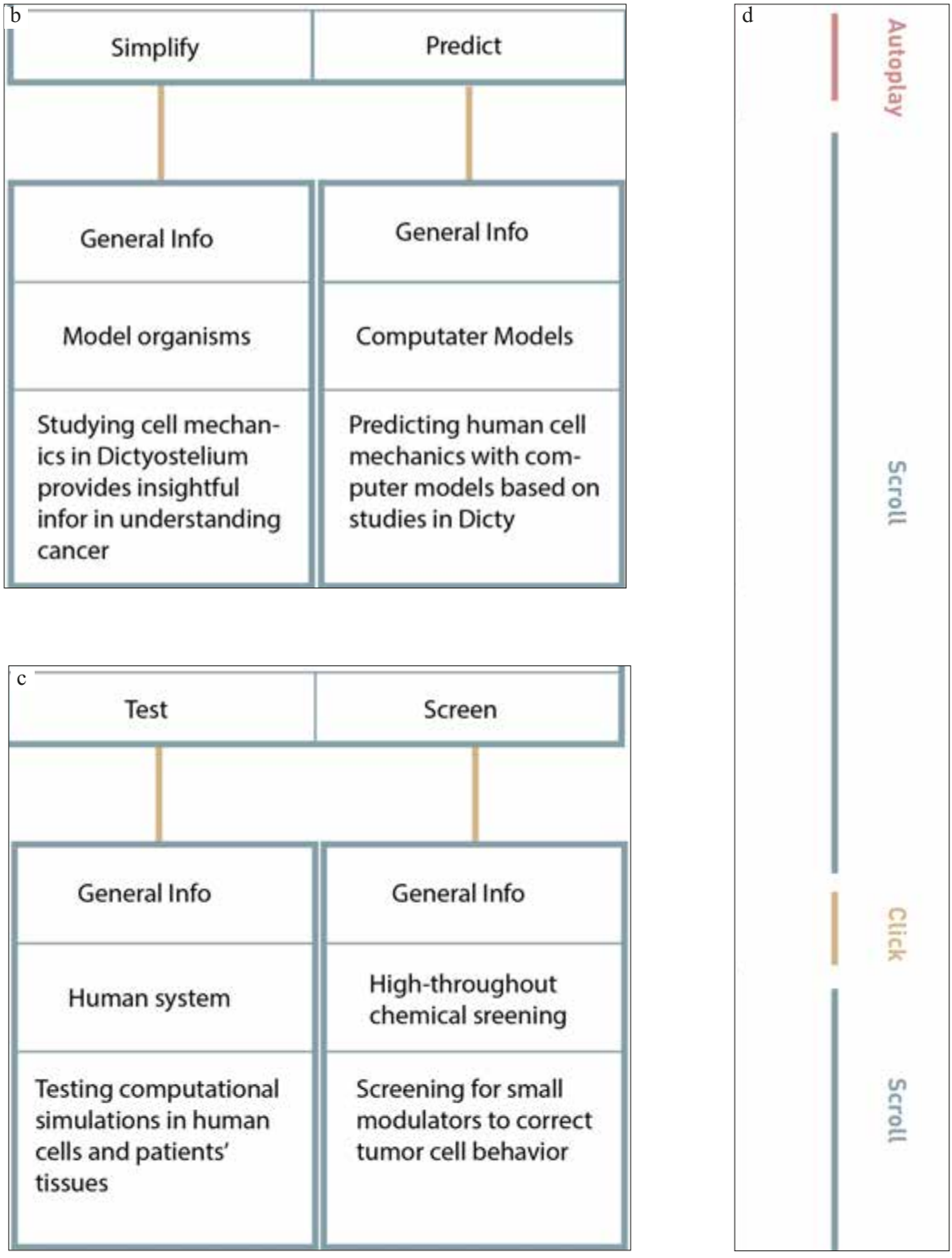


Figure 12b. Finalized flowchart part 2. Child pages Simplify and Predict. **12c. Finalized flowchart part 3.** Child pages Test and Screen. **12d. Finalized flowchart part 4.** User interactivity design.

Storyboarding and Layout Design Process

Storyboards (**Fig. 13**) were created based on the wireframe and word story to show the layout design and intended transitions between various scenes and pages. Storyboards were created using iPad Procreate and were easily exported and modified. The storyboards were shared and discussed with thesis advisor David. Rini, preceptor Douglas Robinson, and other members of his lab to collect feedback on the accuracy and flow of the information. A final version of the storyboards was developed based on feedback and numerous reviews. (Appendix C.)

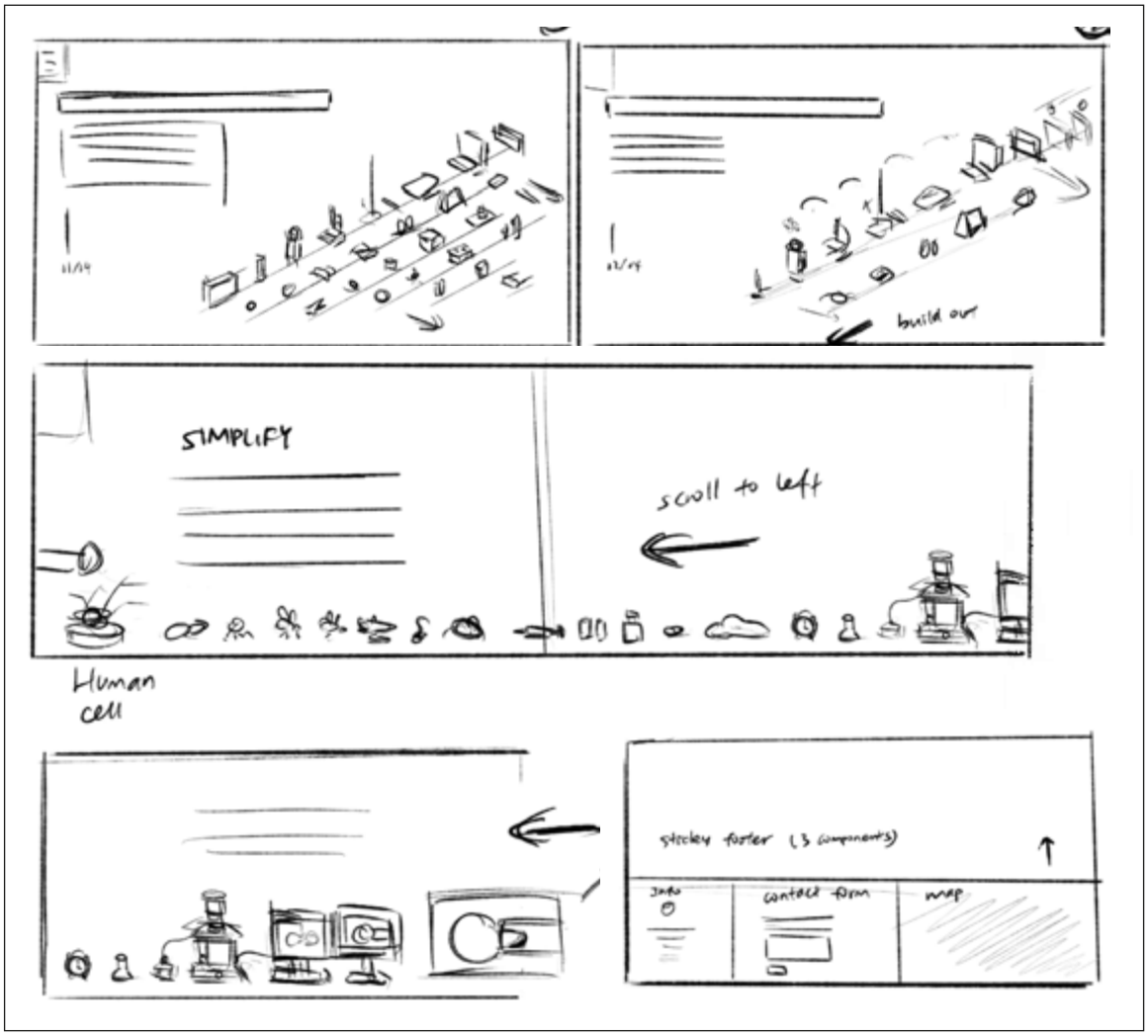


Figure 13. Storyboards development. Text not inteded to be read.

Production Workflow

(1) 3D assets: Draft models and animations were created and key framed based on the storyboards and rendered with basic lighting and materials.

(2) 2D motion elements were created in Adobe After Effects.

(3) User interface designs were produced in Adobe Illustrator.

(4) Animatics (draft prototype) were created in Adobe After Effects.

(5) Feedback was collected throughout the process.

(6) Final renders of 3D assets were set up with well designed lighting and materials.

(7) Animated video was created in Adobe After Effects.

(8) Development of scrolling video site with Scrolling triggered Video Playback technique in JavaScript, and HTML Canvas.

(9) Long-term feedback will be collected through the Contact Form on the website.

List of Softwares
Maxon Cinema 4D
Adobe After Effects CC
Adobe Illustrator CC
FormatFactory
Keynote
Procreate

Figure 14. List of software used.

3D modeling with Maxon Cinema 4D

The majority of the visual elements are 3D models created in Maxon Cinema 4D. A style was developed to match the overall program design with particular consideration given to modeling and render requirements.

(1) Low-polygon modeling

The models were created in a Low-Poly style utilizing the Polygon Reduction deformer (**Fig. 15**). Phong tags were removed or the "Phong angle" was turned down to "20 degree".

(2) Isometric projection with camera setting

Isometric projection shows the depth of 3D objects without foreshortening or distortion. Isometric projection was applied to the models by setting the projection of the 3D camera to "isometric" (**Fig. 16**). Note that the camera can not be rotated once isometric projection is on.

Figure 15. Polygon reduction. Deformer settings.

Figure 16. Isometric projection. Camera set up.

3D simulations with Maxon Cinema 4D

All 3D animations were completed in C4D, using simulations, dynamics, MoGraph and deformers. In addition, some animations required limited keyframes.

(1) **Cellular simulation with displacer**

The simulation (**Fig. 17**) is composed of a sphere and multiple displacers, organized under a single null object. Turning one or a combination of displacers on and off produced different textures on the cell surface, resulting in effective simulations of cellular deformation to represent healthy and infected cells. Subdivision Surface was applied to the folder to smooth the cell surface during the animation.

Figure 17. Cellular simulation settings. A combination of multiple displacers .

Displacer (**Fig. 18**) is a deformer in Cinema 4D that applies noise patterns to the surface of an object to produce an organic look. The noise pattern "Voronoi 1" was selected in this case. Color 1 (originally black) and 2 (originally white) were reversed to further highlight the valleys and ridges of the pattern mapped onto the cell surface. Animation speed was set at 0.5 - 2.5 to allow the cell to change shape without keyframes. A global scale of "600-1000%" was set to make the noise pattern look more subtle. Displacer height, which determines the overall strength of the deformer was set to "10-20 cm". The final result was an organic, bumpy appearing cell.

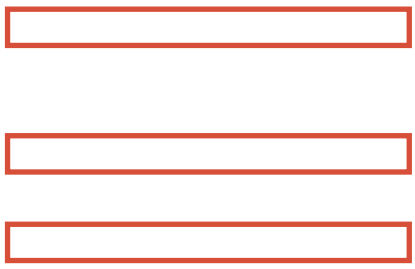


Figure 18. Example of Displacer settings. Height, noise pattern, global scale and animation speed were explored and tested.

(2) Cell tearing simulation with Cloth Simulation tags

The simulation (**Fig. 19**) is composed of a cell (textured with displacers as previously mentioned), with two smaller spheres inside, serving as the forces that tear the cell apart. "Cloth Surface" was applied to the cell, providing thickness. The spheres were set as "Icosahedron" and "Render Perfect" was unchecked. "Subdivision Surface" was then applied to smoothen the polygons during tearing.

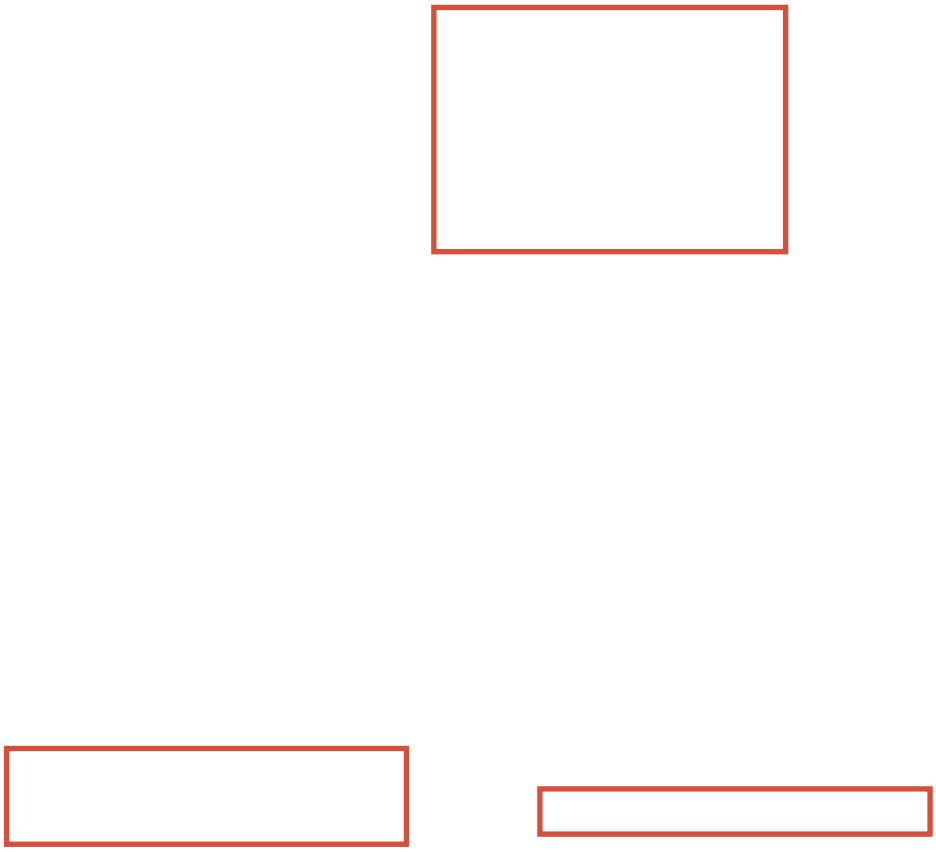


Figure 19. Cell tearing simulation. Cloth Surface, Subdivision Surface and force generation.

The positions of the spheres were keyframed to move outwards and generate the force that tears the cell apart (**Fig. 20**).

Figure 20. Generating force. Keyframe the positions of the spheres along the timeline.

Simulation tags (**Fig. 21**) were then applied to the objects. Cloth Tag (tag > simulation tags > cloth tag) was applied to the cell. "Use Tear" was checked and "Tear" was set to 160%. Gravity was set to "zero" so the cell did not fall. The "cell" was made "Editable" to ensure the smoothness of the tearing simulation. Cloth Collider Tag (tag > simulation tags > cloth collider tag) was applied to the small spheres with the default settings.

Figure 21. Simulation Tags settings. Cloth Tag and Cloth Collider Tag.

(3) Cell deformation and movement using soft body dynamics

This simulation (**Fig. 22**) is composed of 13 spheres (cells), in a cube acting as a bounding box. Turbulence was added to the scene, providing the external force for cells to move randomly. The spheres were positioned as close to each other as possible. Note that the spheres should not touch each other at frame zero, otherwise C4D might crash.

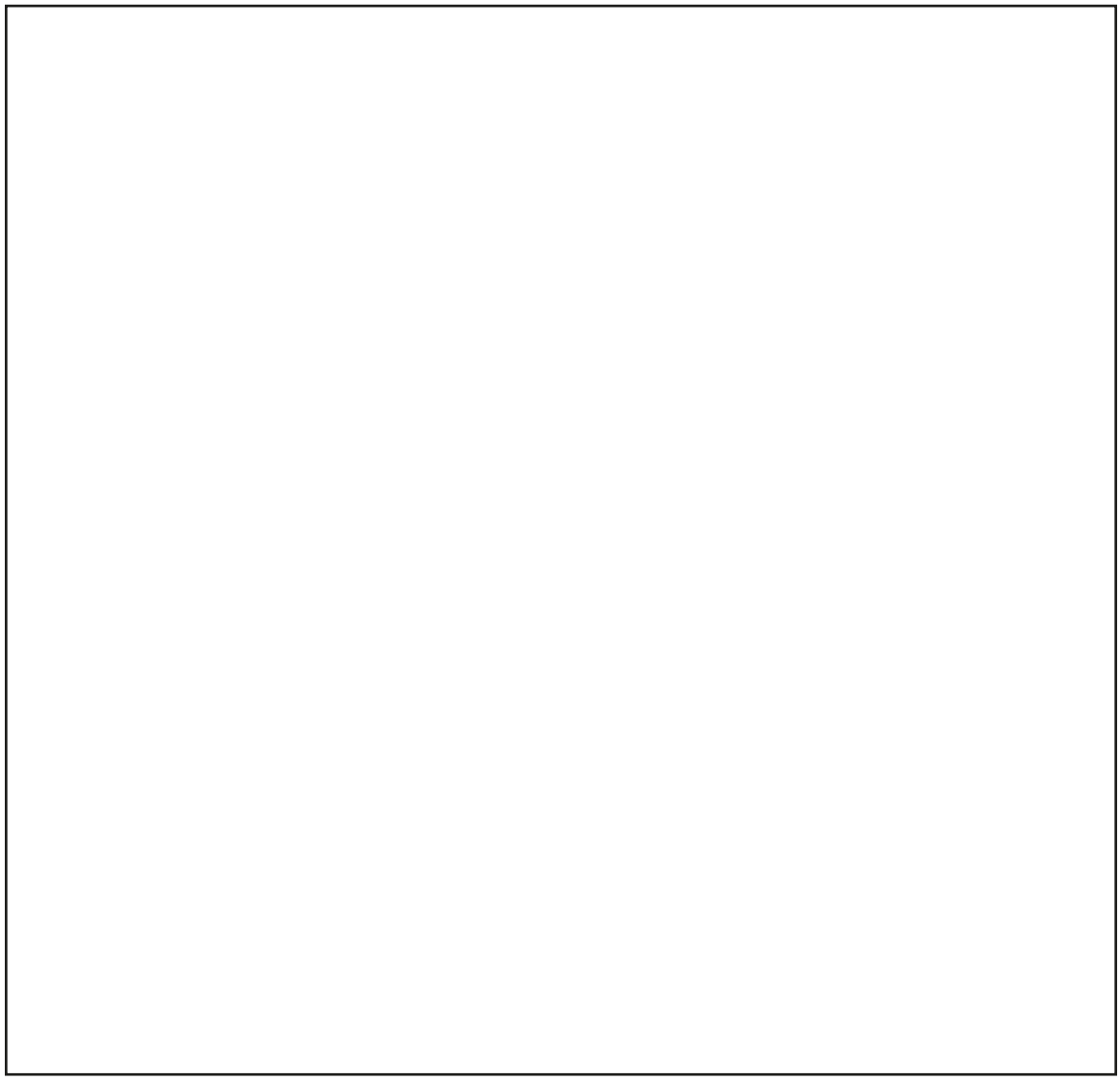


Figure 22. Cell deformation simulation. Multiple spheres inside a cube.

Soft Body Tags (**Fig. 23**) were added to all the spheres. Parameters including structural spring, stiffness and pressure were adjusted to achieve the desired cell deformability. “Pressure” makes the cells expand like balloons to fully occupy the volume of the bounding box once hitting the play button. This causes the cells to squeeze together and interact with each other.

Figure 23. Soft Body Dynamics. Structural, Stiffness, Pressure.

Collider Body Tag (**Fig. 24**) was added to the cube. “Static Mesh” was selected under Shape.

Figure 24. Collider Body Simulation. Static Mesh.

Gravity of the 3D world was adjusted under Project dynamics (Cmd + D). from the default of 1000cm to 10cm to prevent the objects from falling. Turbulence (Simulate > Particles > Turbulence) was applied to the scene. Scale and Frequency were set to 100% in this case.

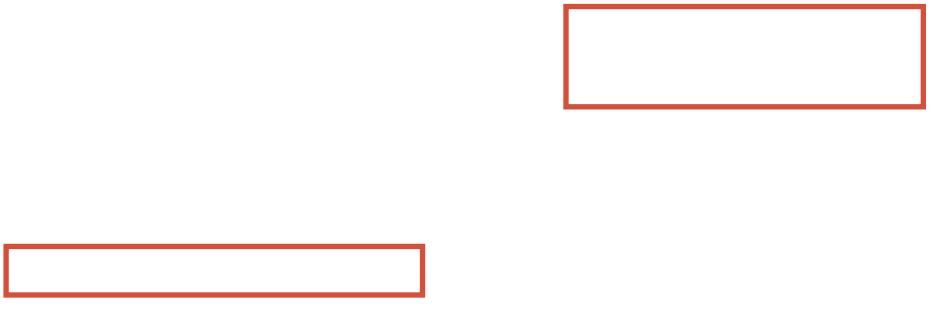


Figure 25. Gravity and Turbulence. Reduce Project Gravity, increase Turbulence Strength and Scale.

(4) DNA helix winding with twisting

The simulation (**Fig. 26**) is composed of straight splines that represent the backbone and base pairs of the DNA helix. Each spline is a child of a Metaball. The Hull Value and Subdivision level are shown below. One of the base pairs was separated from the main spline to receive materials with different colors, representing gene mutation. Twist deformer was applied to each spine. The angles (0 - 720 degree) were keyframed to animate the winding and unwinding process of the DNA double helix.

Figure 26. DNA helix simulation. MetaBall and Twist Angle.

(5) Slime Mold movement with Metaball, Metaball tag and MoGraph

This simulation (**Fig. 27**) is composed of a static plate, and a dynamic "slime mold", consisting of a clone of spheres, and a cylinder to represent "agar", which are children of the same Metaball so that the "agar" will move along with the Cloner when acted on by the Formula effector.

Figure 27. Slime Mold Movement. Cloner, Metaball, Formula.

Metaball is effective on spheres and splines, but often does not work consistently with shapes like cylinder or cubes. Hence, a Metaball tag (Tags > Cinema 4D Tags > Metaball Tag) was added to the cylinder to achieve a better result. Strength and Radius were set to 55% and 15cm, respectively.

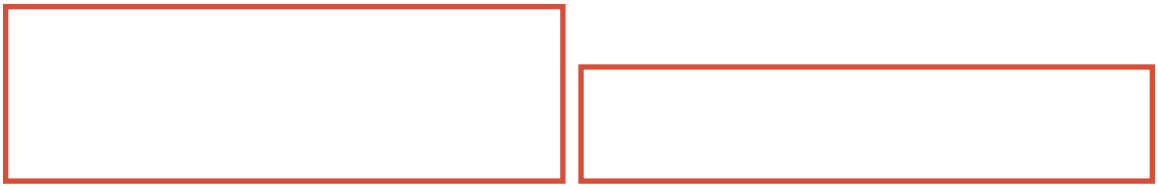


Figure 28. Metaball and Metaball Tag. Hull value, Subdivision, Strength, Radius were adjusted.

MoGraph is a toolset in C4D that creates various motions effects. The basic shape of the "slime mold", was created using the Cloner (MoGraph > Cloner > Grid Array) (**Fig. 29**), which was animated with MoGraph effectors. A Formula (**Fig. 30**) effector was used in this case, and a Sin wave was applied.

Figure 29. Cloner settings. Grid Array.

Figure 30. Formula Effector settings. Sin wave.

Lighting and Materials

Lighting

To achieve a clean style without dramatic shadows, **Illuminati** (**Fig 31**), a free plugin, was used to light up the entire scene. **Light intensity** was set to between 50 - 60% to prevent overexposure. Inner and outer **angles** were adjusted to show details in the shadows.

Figure 31. Illuminati settings. Noted that Illuminati renders much faster than Global Illumination.

Materials

Materials for most objects were kept simple with only Color and Reflectance channels turned on. The color was set to 80-100% white. Specular strength and width were adjusted to provide a slight shininess. Settings are shown below (**Fig. 32**).

Figure 32. Material settings. Only Color and Reflectance channels were turned on. Noted that "V" of the Color channel was adjusted from 85% - 100% for different objects to avoid overexposure on some objects that have more polygons directly facing the light.

Render Settings

The Physical Renderer (**Fig. 33**) was used to render all the 3D objects, animations and scenes. The sampling quality was set to Medium, which improved the the final appearance compared to Low, and rendered much faster than the High setting. Output was set to 1280 (Width) x 720 (Height) pixels with the resolution of 180 DPI. Ambient Occlusion (AO) was added, cached, and rendered on a separate layer. The maximum ray length was increased from the default of 100cm to 150 - 200cm to intensify the soft shadows that occur in the crevices of the objects and the planes where the objects touch the floor. The color was changed from black to dark blue to match the background color.

Figure 33. Render settings. Physical Render and Ambient Occlusion.

Render with Take System

Cinema 4D's Take System (**Fig. 34**) was used to render multiple objects separately from the same file. Each "Take" stores any action applied to the objects, including turning the visibility on and off, adding tags and changing camera angles. Note that that relevant Take must to be selected in order to change the settings,. In this way, objects can be automatically rendered one after another by indicating the Takes to be rendered (**Fig. 35**). In addition, Takes can be set as a Child of another Take (**Fig. 36**), to inherits the actions from its Parent.

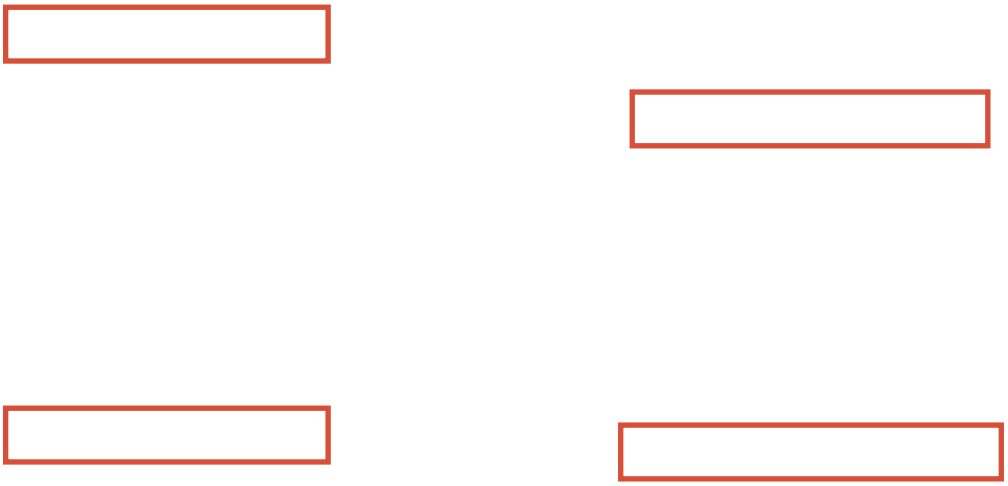


Figure 34.Take System. Create new Takes and store the visibility of each object accordingly.

Figure 35. Mark the Take. Rendered Marked Takes to Picture Viewer.

Figure 36.Child Take. Inherit settings from its Parent Take.

Specific render settings can be assigned to each take (**Fig. 37**), whether it is a static or an animated object. Different render variables (Output, Ambient Occlusion, etc) were set up and saved with specific labels under Render Settings. Then a list of these already saved Render settings was displayed in the Take manager, which could be assigned to the Takes, respectively.

Figure 37. Render settings assigned to Takes.

User Interface Design in Adobe Illustrator

2D and 3D assets and draft renders (if not finalized) were imported into Adobe Illustrator to develop the user interface design (**Fig. 38**). The visual elements and text were composed on multiple Artboards and layers. Artboards allow the presentation of the interface designs for each page all at once to ensure consistency of the style. This method allows the text layout to be directly copied and pasted into Adobe After Effects text layers, keeping the character style consistent, thereby streamlining the workflow.

Figure 38. An example of Adobe Illustrator Interface. Multiple artboards and layers created for the user interface design. Text not intended to be read.

2D motions with Adobe After Effects

2D motion elements were added to the design to deliver information and guide the viewers through the interface. All of these elements were created in Adobe After Effects (AE).

Trim Paths (**Fig. 39**) was used to efficiently animate line motions without using masks. The Animated icon“ Scroll to explore” was created this way. Trim-path was added to the layer by > Shape Layer > click the play button next to “Add:” > choose “trim paths”. “Start” and “End” were adjusted between 0 - 100 %. Keyframes were set for “Start” and/or “End” to create the desired motion.

Figure 39. Animated Icon created using Trim Paths. Start and End features were key framed.

Creating Animated Prototype in After Effects and Keynote

Animated prototype was created in After Effects (**Fig. 40**) for pre-visualizing the interactive design, including pacing, the flow of the information, and the overall effectiveness of the motions. Images, texts composed in Adobe Illustrator, as well as PNG sequences (**Fig. 41**) rendered in C4D, were imported into Adobe After Effects.

Figure 40. Example of the After Effects workstation. Text not intended to be read.

Figure 41. Import PNG Sequence. Animations rendered in C4D and exported as PNG Sequences.

Loop Animation with Time Remapping and After Effect Expression

Animations created in Cinema 4D were rendered with a limited number of frames in the form of PNG sequences. After Effects allows looping of these animations (**Fig. 42**).

PNG sequences imported into an After Effects composition show as an individual layer. Time Remapping can be activated by right clicking the layer > choose Time > Enable Time Remapping. This will add the Time Remap feature to the timeline. Alt click on the "clock" icon next to "Time Remap" opens the Expression menu > click the play button next to "Add:" > choose property > LoopOut > drag the end of the timeline to loop the animation for certain amount of time.

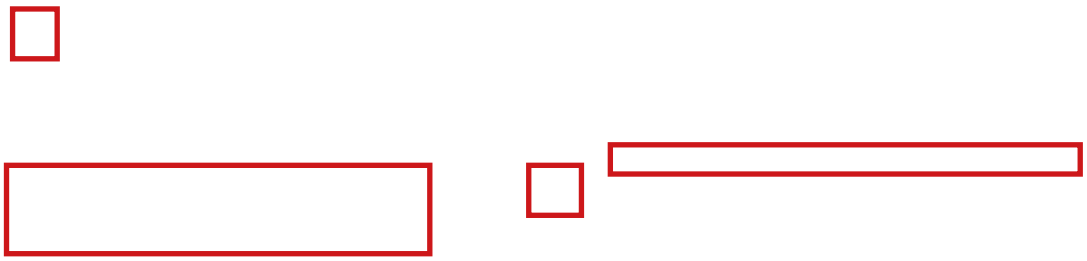


Figure 42. Loop animation. Time Remapping and Loop Out expression.

Test motions in KeyNote

Keynote was used to quickly test the effectiveness of text transitions and movement of the images, before proceeding to After Effects. Under the "Animate" tab, there are three types of object-based animation presets: "Build In," "Actions" and "Build Out.", and one set of slide-based animation, such as Magic Move (**Fig. 43**). "Move" (Action > Move) was applied to the images to achieve horizontal scrolling effect. "Dissolve" (Build In/ Build Out > Dissolve) was used to fade the paragraphs in and out. The animations were then arranged in a specific order by setting up the "Build Order" (**Fig. 44**).

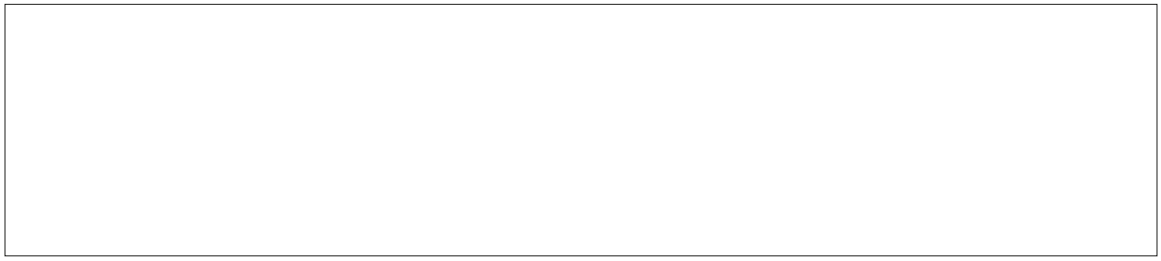


Figure 43. Animate in Keynote. Animation Presets include Page Transitions, Build In, Action, Build Out.

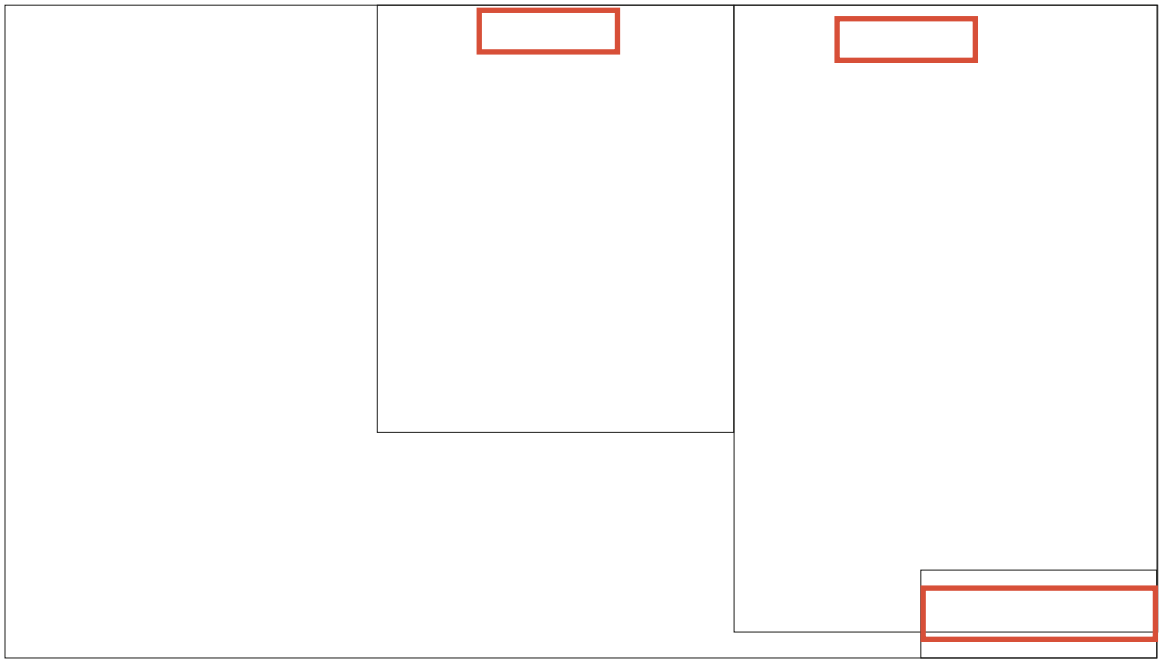


Figure 44. Example of Keynote interface. Not all text is intended to be read.

Scrolling Triggered Video Playback with JavaScripts

The final animated video was created based on feedback of the animatics. The video, audio and other related files were well-labelled and organized in a single folder. Pre-written JavaScript and HTML scripts were applied to the files, to control the progress of the video in response to "scrolling". This technique, called "scrolling triggered video playback", enables self-paced control of the video through scrolling up and down in the browser.

The alpha version of the codes, referred to as "Scrolleo" (Scrolling + Video) by the author, was created and shared by Mark Teater on CodePen and GitHub (**Fig. 45**). The codes were tested locally, customized and combined with HTML canvas animation and elements. JavaScript, HTML and CSS scripts are attached in the Appendix D and E, respectively.

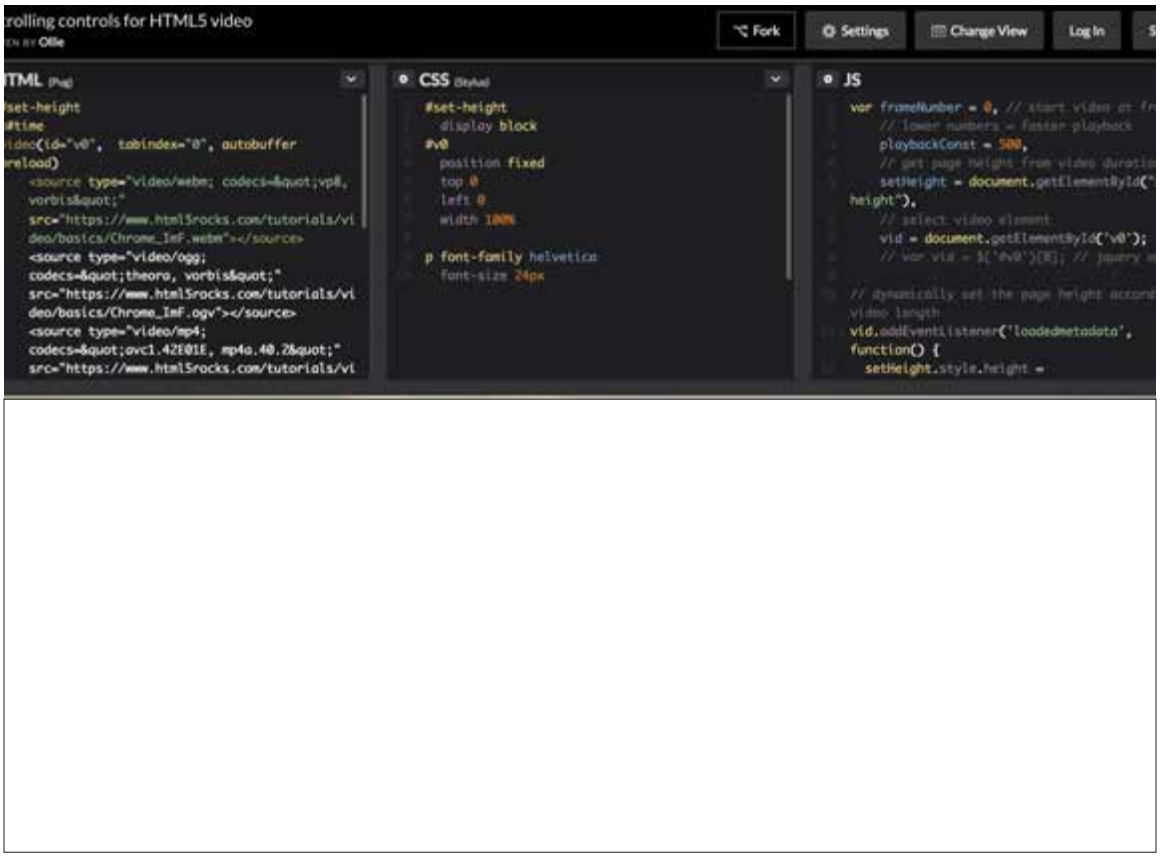


Figure 45. Example of CodePen and GitHub interfaces. The alpha version of Scrolleo was introduced and shared on these open sources by the author Mark Teater. Text not intended to be read.

The general mechanism (**Fig. 46**) of the script is to link the video duration (temporal measurement) into the document height (spatial measurement), using Javascript functions (document.height = Math.floor(videoDuration) * scrollScale + "px", scrollScale is a fixed factor that determines how many frames to play when scrolling once). When the scroll bar reaches a predetermined height, the browser obtains the scroll height, translates the height back to the temporal measurement, and returns the video current time. (Video.currentTime = (scrollHeight/ document Height) / scrollScale).

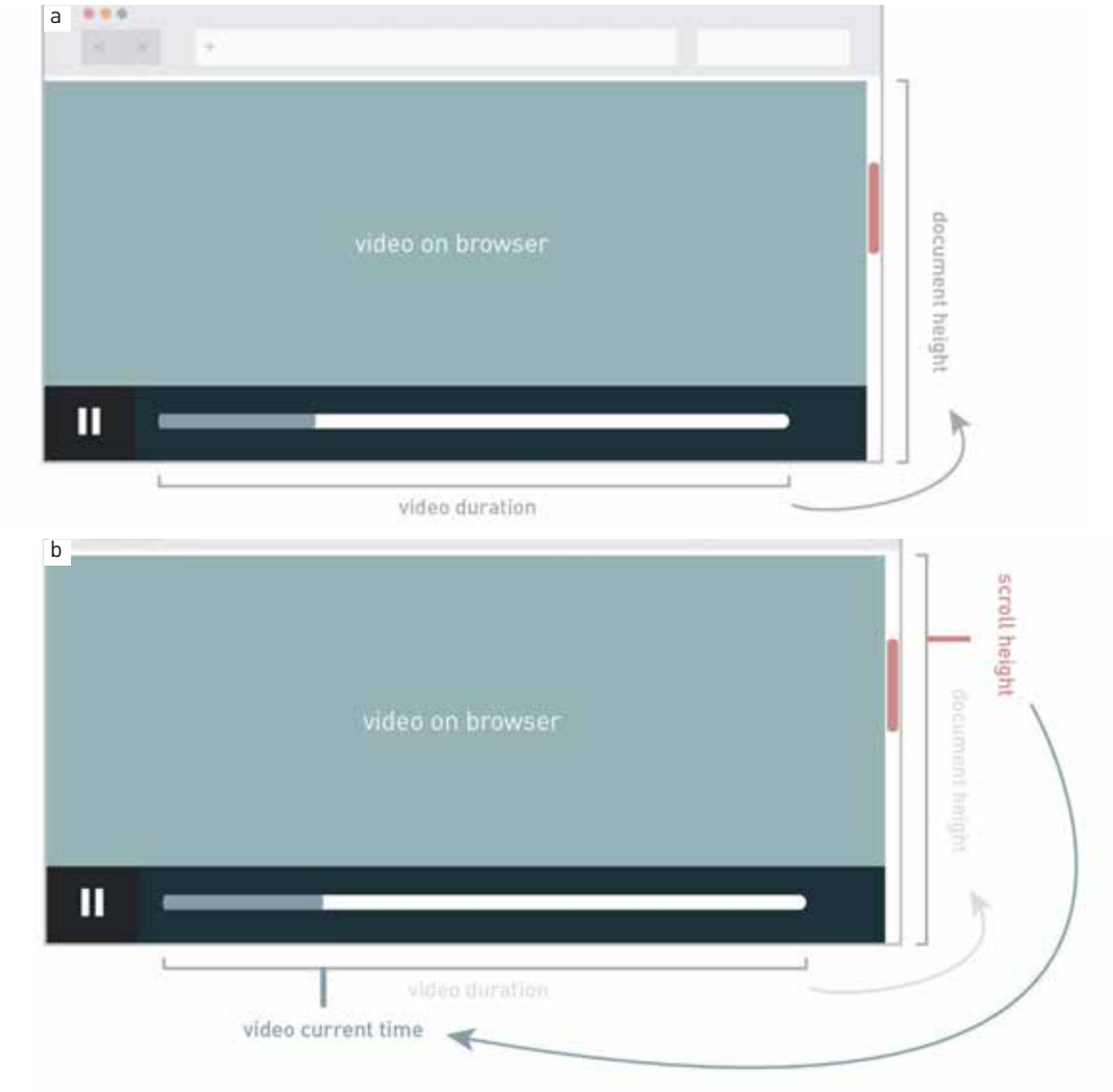


Figure 46. Javascript Mechanism. a, step 1. Conversion of the video duration into the document height. **b, step 2.** Translation of scroll height back to video current time.

Several other factors were taken into consideration to ensure a smooth scrolling experience:

(1) Format Conversion

The animated video exported from After Effects is a MOV file, which is not the most compatible format for browser-based presentation. Format Factory (**Fig. 47**) was used to convert the MOV file into an MP4 file. The MP4 video was then converted and compressed into Webm format, which compressed the video size by 10 times with only a slight compromise of the resolution.

Figure 47. The interface of Format Factory. Not all text is intended to be read.

(2) Keyframe setting

To ensure that the scrolling playback is not choppy each frame must be set as an individual keyframe. This gives each frame equal weight and forces the browser to show every frame as scrolling, instead of skipping between keyframes that may be too far apart.

(3) Browser optimization

Various browsers have different rules to define property of HTML labels. Some consider that HTML header do not take space so the document height is determined by the Body. While others take all document elements into account. To ensure compatibility across different browsers, both rules were considered when calculating the document and window height (**Fig. 48**).

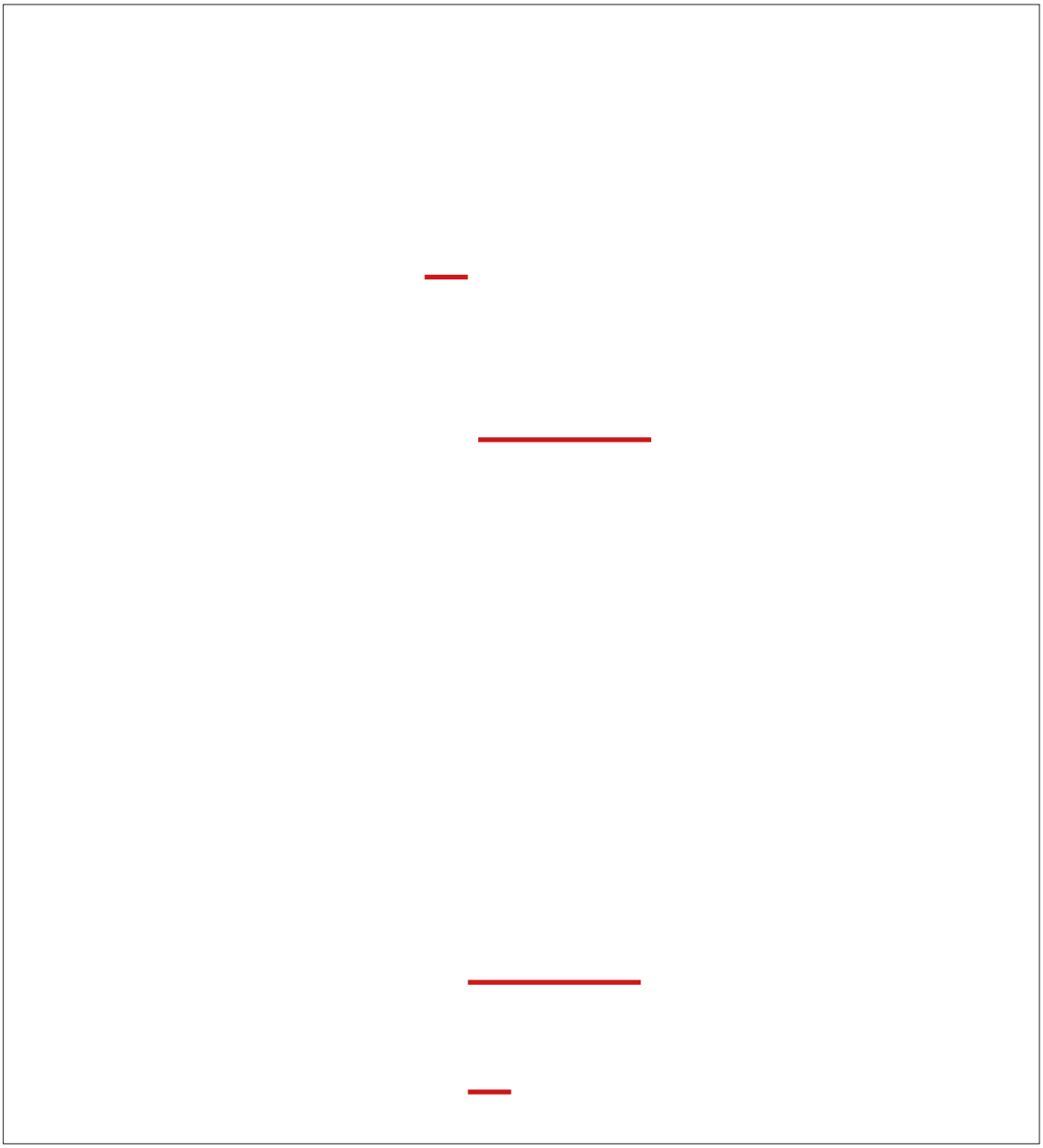


Figure 48. Section of the script. Compatibility across browsers was taken into account.

Design Concept

This web-based public outreach program developed during the course of the thesis communicates information about the critical role of fundamental research in human health. The thesis focuses on both written and artistic approaches of conveying advanced concepts. This includes the development of the word story, 3D models and animations, 2D motions, as well as user interface and experience design. An interactive website (**Fig. 49**) is under development to embrace the word story and artworks in a visually pleasant and easy-to-follow manner. The website will host five full-screen interactive videos to walk the audience through a storyline that helps communicate the concept, "what can fundamental research do for you?".

One key development of the program was the incorporation of a specific technique, namely "Scrolling Triggered Video Playback" into user interactive design. This JavaScript coded interactivity gives users full control over the progress of the animated video. The intuitive nature

Figure 49. An example of the user interface on the local browser and a list of the working files.
(video size: 1080 x 720; video frame rate 30 fps. video format: webm) Not all text is intended to be read.

of scrolling up and down prevents the audience from getting lost or being overwhelmed by buttons and hyperlinks while they are navigating through the site.

A second aspect of the program focuses on the consistency of the user interface design that is expressed across the following design attributes:

(1) **Color, size and shape**

This was achieved by first developing the color scheme (**Fig. 50**). The color scheme of the user interface was designed to be clean, calm and professional. Five main colors were chosen: blue as the background color; white with a silver tint as the main color for the 3D models, supplemented with red, yellow and green. Second, DIN Pro was chosen to be the typeface across the site. Font sizes of the title, body text, menu and page numbers were set up to build the hierarchy in reading and kept consistent throughout the program. Additionally, consistency of the design elements, such the thickness of the strokes, was paid attention.

Figure 50. Color scheme. 3D and 2D color palettes.

(2) Content and Imagery

3D models, animations and 2D assets (**Fig 51-54**) have a stable and consistent style.

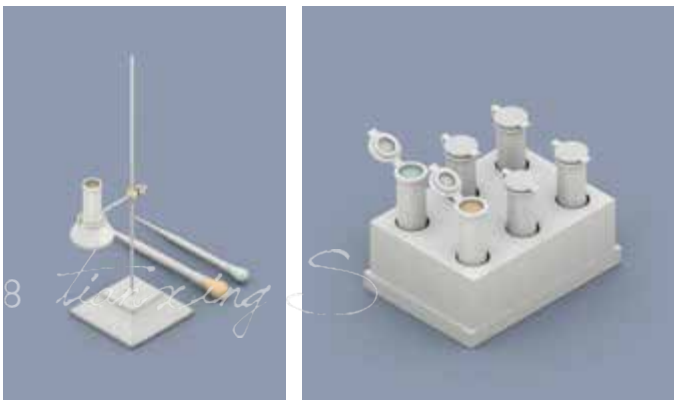


Figure 51. 3D assets 1. Research and medical devices.

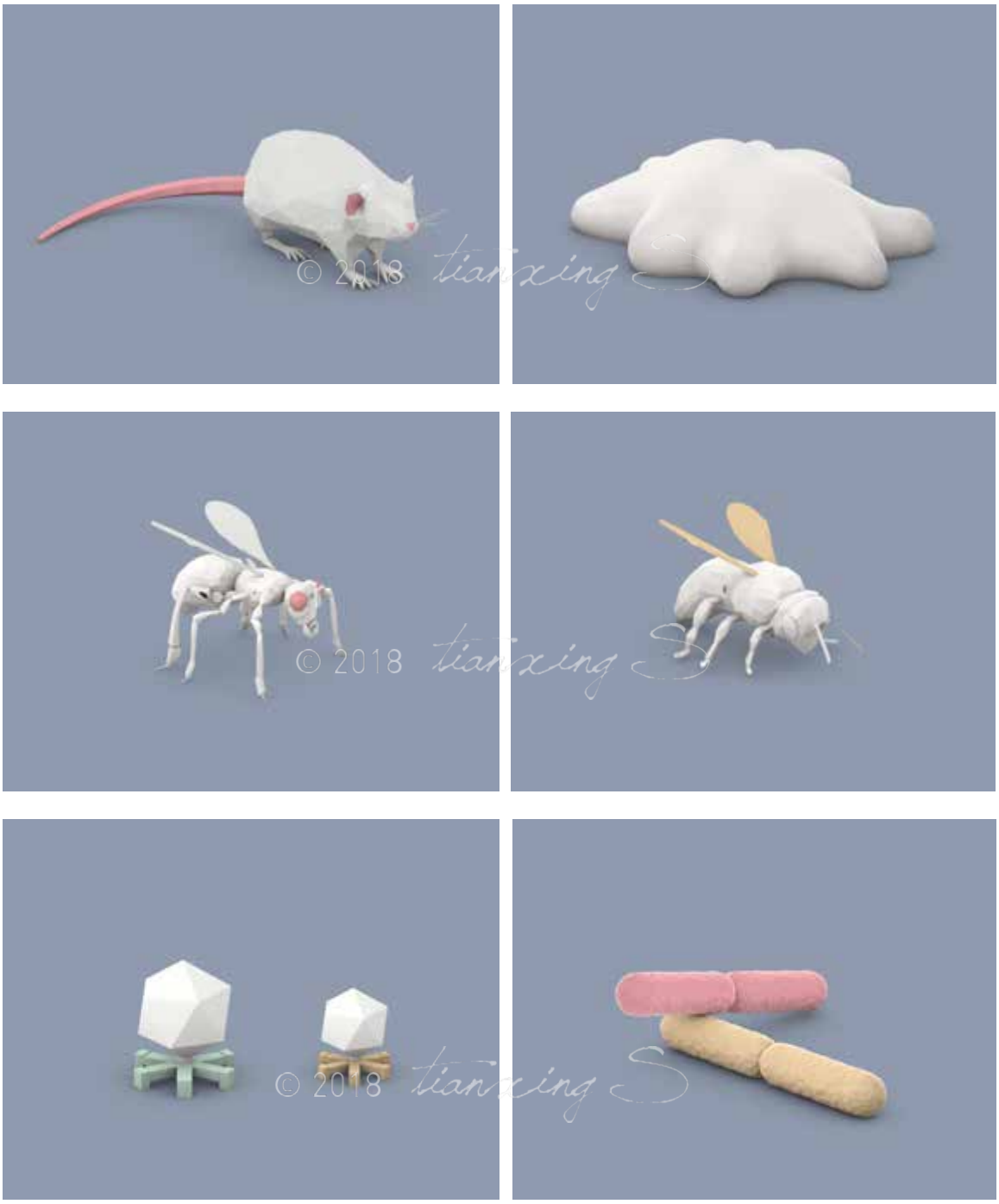


Figure 52. 3D assets 2. Research model organisms.

Figure 53. 3D assets 3. Research instruments.

Figure 54. 2D art assets. 2D animation of Micropipette aspiration (MPA).

(3) Layout

Three master layouts were created for the compositions of the videos. The position and volume of the paragraph were designed based on the amount of written information to be presented.

Layout 1 Main page | Video 1: Intro part 1-2 (Fig. 55)

Background information on current health challenges and fundamental biomedical research is presented in short paragraphs at the upper left corner of the screen. The isometric design is intended to create a visual sense of the research world in a simplified and pleasant way.

Figure 55. Layout 1. Introduction part 1-2. Text not intended to be read.

Layout 2 Main page | Video 1: Intro part 3-4 (Fig. 56)

As more advanced concepts are introduced, such as the challenge in experimental design, the space taken by the imagery is reduced and positioned to the center, longer paragraphs are presented and placed under the imagery. It is designed to minimize distraction so that viewers could explore all the information by focusing on the center portion of the screen.

Figure 56. Layout 2. Introduction part 3-4. Text not intended to be read.

Layout 3 Child pages | Video 2-5: Research strategy 1-4 (Fig. 57)

Four research strategies are further explained through four videos on separated pages that are linked to the main page. The visual elements are further reduced in size and positioned to the lower one third of the screen, leaving more space for the word story. As users scroll, visuals move from right to left, introducing new elements to help explain the information.

Figure 57. Layout 3. Child page 1 "Simplify". Text not intended to be read.

(4) User interactive pattern

The interactive pattern (mostly scrolling) is kept simple and consistent throughout the site, guided with clear instructions (**Fig. 58**). The animated icon "scroll to explore" appears when the users are about to finish the current section. Underline indicates that the element is clickable. Page navigation elements, including page numbers, and a progress bar are presented at the same location across each page to indicate users about how much they have achieved and how much more to expect.

Figure 58. Instructions. Animated icon "Scroll to explore"; clickable "underline"; page navigation.

User Interface Design

Screen-captures of the user interface design can be found on the following pages (**Fig. 59 - 75**).

The texts in the images are not intended to be read.

Figure 59. Loading page design. Loop animation of amoeboid movement.

Figure 60. Landing page design. Opening: How does fundamental research help you?

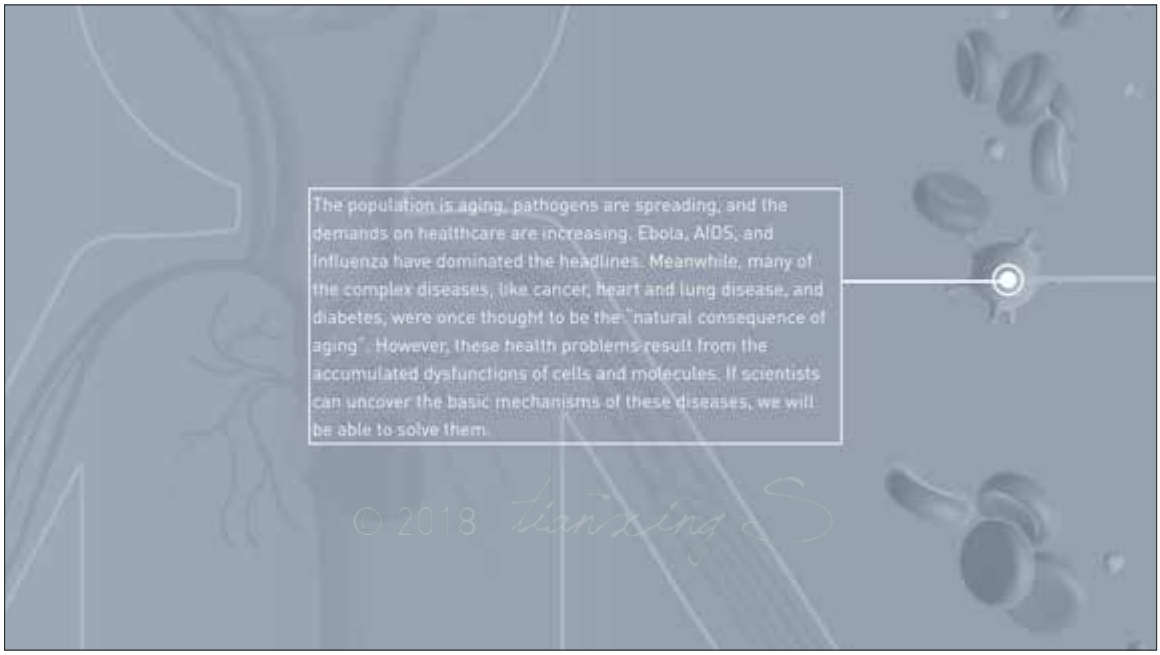


Figure 61. Main page design 1. Introduction part 1: current health challenges. Noted that the text is not intended to be read.

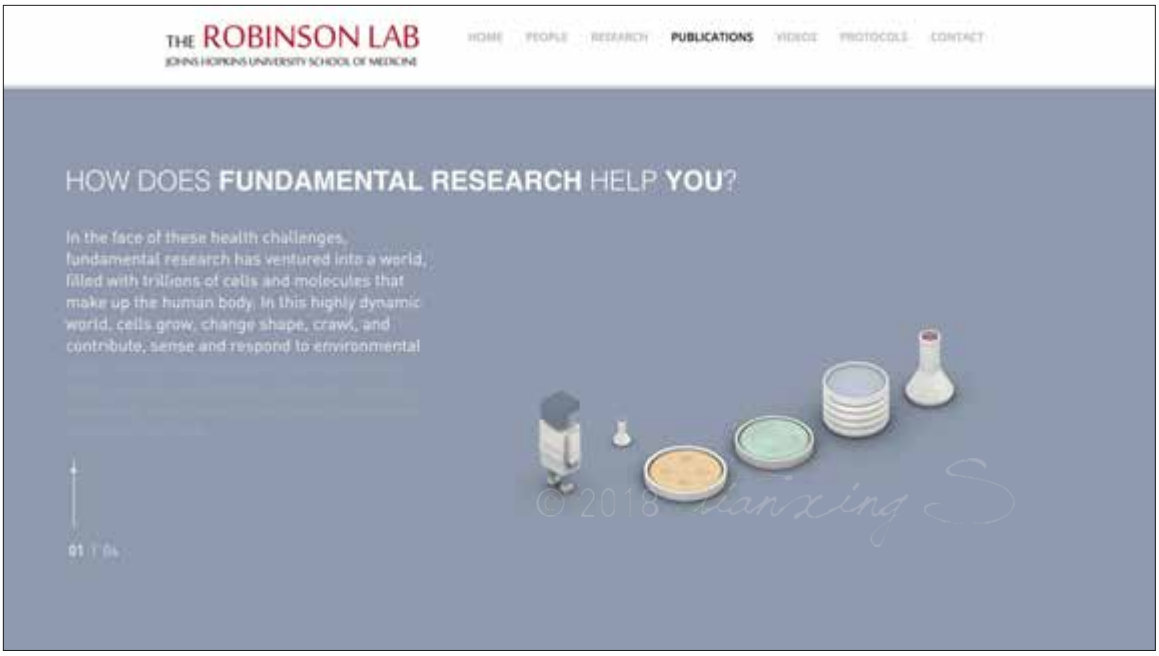


Figure 62. Main page design2. Introduction part 1: In the face of current health challenges, fundamental research has ventured into a highly dynamic world of cells and molecules that make up the human body. Noted that text included in the image is not intended to be read.

Figure 63. Main page design 3. Introduction part 1: While medical breakthroughs are made possible along the research process, researchers are poised to expand our understanding of the cellular and molecular behaviors involved in various diseases in order to create even better treatments. Noted that text included in the image is not intended to be read.

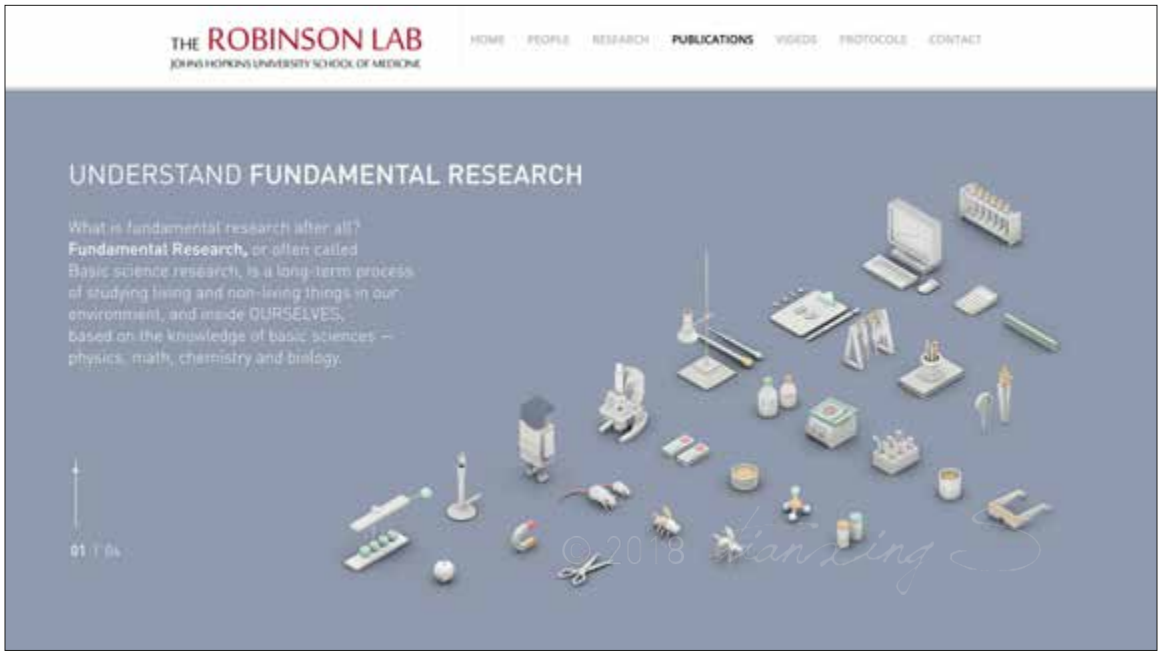


Figure 64. Main page design 4. Introduction part 2: what is fundamental research after all? Noted that text included in the image is not intended to be read.

Figure 65. Main page design 5. Introduction part 2: general flow of doing research. Noted that text included in the image is not intended to be read.

Figure 66. Main page design 6. Introduction part 3: There is still so much we do not know about various diseases like cancer, heart disease, COPD, and diabetes. Before we can cure diseases, researchers are seeking for answers to many basic questions, such as, why cells move? how do they communicate amongst themselves? The answers will lay the foundation for understanding biology of various illness. Noted that text included in the image is not intended to be read.

Figure 67. Main page design 7. Introduction part 3: Finding the answers to these basic questions, however, is greatly hindered by the extreme complexity of the human system. Direct experimental designs are not only difficult, but also time-consuming and economic-inefficient. Noted that text included in the image is not intended to be read.

Figure 68. Main page design 8. Introduction part 4: to save time, materials and money, scientists have developed various strategies. Here we present a workflow based on research projects carried out in the Robinson Lab in the Department of Cell Biology at Johns Hopkins University School of Medicine. Noted that text included in the image is not intended to be read.

Figure 69. Main page design 9. Introduction part 4: the workflow is generalized into a series of four strategies, namely simplify, predict, test and screen. Users can click on each one to read more. Noted that text included in the image is not intended to be read.

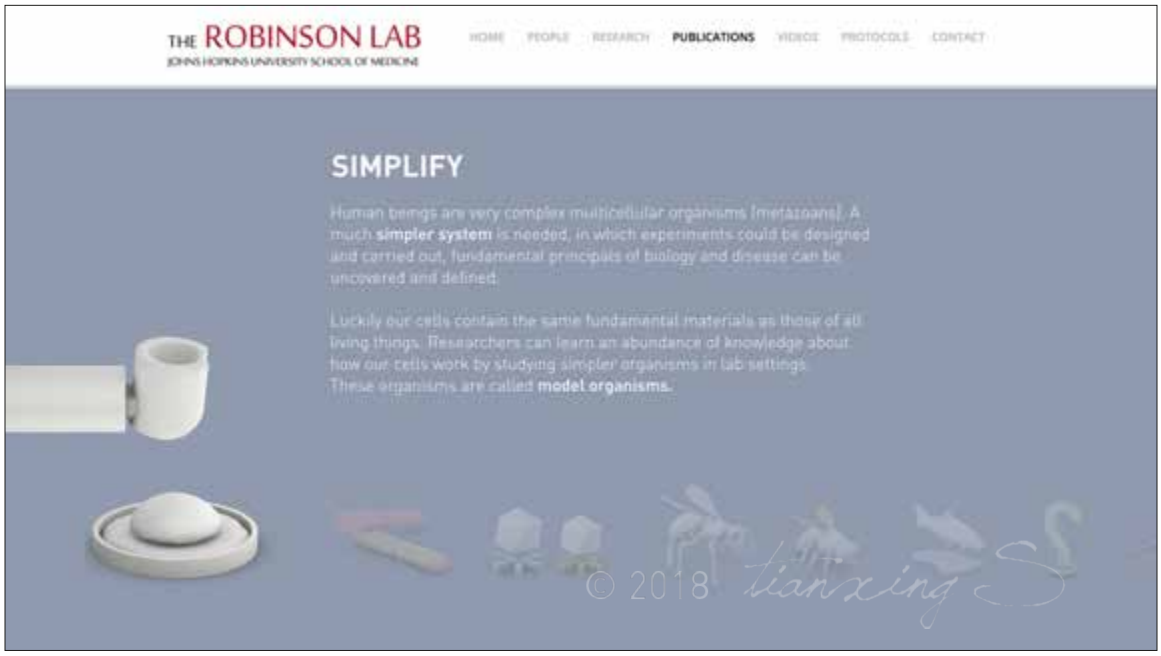


Figure 70. Child page design 1. Simplify: human beings are very complex organisms. Simpler model organisms are studied in lab settings, in which fundamental principles of biology and disease can be uncovered and defined. Noted that text included in the image is not intended to be read.

Figure 71. Child page design 2. Simplify: classic model organisms include E.coli, Phage, fruit fly, honeybee, zebrafish, worm and mouse. Noted that text included in the image is not intended to be read.

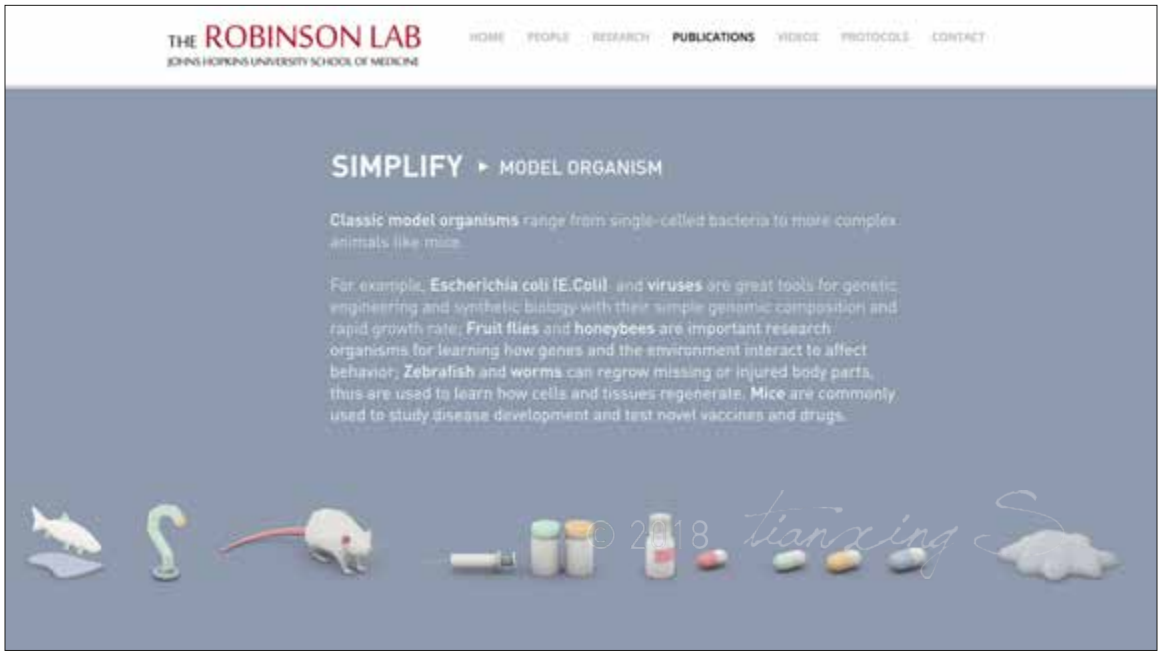


Figure 72. Child page design 3. Simplify: the end of "classic model organisms". Dictyostelium is about to show up. Noted that text included in the image is not intended to be read.

Figure 73. Child page design 4. Simplify: Common feature of Dictyostelium and its role in studying various human diseases. Noted that text included in the image is not intended to be read.

Figure 74. Child page design 5. Simplify: studies in Dictyostelium conducted in the Robinson Lab revealed cellular behavior and protein dynamics involved in cancer metastasis. Noted that text included in the image is not intended to be read.

Figure 75. Sticky footer design. Contact information, contact form and map. Noted that text included in the image is not intended to be read.

Asset Referral Information

The animated videos can be reviewed at:

http://robinsonlab.cellbio.jhmi.edu/videos

The scrolling video site can be accessed through:

http://marytianxing.com/#thesis

A copy of this thesis and all its assets is located in the Johns Hopkins University Department of Art as Applied to Medicine.

DISCUSSION

Fundamental research is a relatively abstract and complex process. The nature of the science itself can pose a major challenge for communication. Diversity in the ways in which people interpret information can add to the challenge. In order to create a successful public outreaching program, several strategies were employed and considerable thought was required to address the challenges of communicating and visualizing fundamental science.

Word Story Development

The development of Word Story, (information presented in the form of a story to help explain complex issues), is a method frequently used by science communicators. (Entwistle et al., 2011; Shaffer and Zikmund-Fisher, 2012). Word Story, sometimes referring to a narrative, can increase audience engagement with and attention to science communication, and be easier to remember and process relative to traditional forms of scientific communication, such as academic literature. (Bekker et al., 2013; Dahlstrom, 2014; Kanouse et al., 2016) The development of the Word Story is the very beginning and probably the most challenging part of the entire project. During this process, A few factors were taken into consideration.

(1) The extensive scientific terms were carefully translated into language the general public could understand or follow. For example, “cell cytokinesis” was replaced by “cell shape control”; “cell cortex” (the structure of the cell, referring to cell membrane and the cytoskeleton network just beneath the membrane) was replaced by “cell skin”. These wording changes were discussed with Dr. Robinson to ensure accuracy while minimizing the jargon.

(2) Since communication that considers people’s challenges with numeracy is generally more effective, (Peters et al., 2007), the numerical information was either coupled with visual

elements to help with the understanding or removed from the story entirely if doing so would not diminish the flow and accuracy of the content. For example, when explaining the use of computational modeling in simulating and predicting human systems, stylistic line graphs with a few dots were used to provide a general sense of statistical information, however, they did not include mathematical information that would require specific knowledge.

(3) The flow of the information was carefully designed and modified based on feedback from various sources, including faculty advisor David Rini, content preceptor Dr. Robinson and other non-scientists reviewers. Firstly, information was presented in small sections, which was intended to give user a break in between sections to process the new information. Second, each section, such as research strategies, was designed to have three layers of information, starting with a very general and brief description, followed by well-defined background information, and finally ending with specific examples.

Choice of Case Study

The study of cell mechanics in cancer treatment was chosen to be the case study to explain research concept and approach for several reasons. First, this research project integrates several subfields from cell biology, protein dynamics, to computational modeling and chemical biology. It follows a relatively linear workflow, which gives the audience a broad view of current biomedical research; Second, the study delivers the message to the audience that model organisms play a key role in fundamental research. The message provides answers to frequently asked questions, such as, why doing experiments in bacteria or animal species that are seemingly very irrelevant to human? Third, the study has great value in medicine and cancer therapy. Topics related to human health and disease prove to be powerful in drawing people's attention. Additionally, the study of cell cytokinesis and mechanosensing is an interesting topic not commonly covered in biology curricula. Though mitosis and cell division is often taught in

basic science education, cytokinesis and mechanosensing involve more advanced knowledge. Further, current approaches to cancer treatment focus on targeting signal transduction pathways. Cell mechanics offers an alternative approach to potential novel therapeutics.
Apart from the development of a narrative Word Story, a few other factors regarding the artistic style, user experience design, feedback collection were also carefully considered, as discussed below.

Artistic Style

(1) Isometric projection

Different from true perspectives, lines under isometric projection do not converge to a vanishing point but run in parallel. This method of visual representation of three dimensional objects is intended to provide the illusion of depth without distortion. Isometric projection is conventionally used by engineers, architects and technical illustrators for easier presentation and measurement of designed products. While the lack of foreshortening of the 3D objects provides a rather clean and consistent looking to the design. This technique, often combined with low-poly modeling (to be discussed later) became popular in the field of graphic and web design, as well as user interaction development in recent years.
In addition to the aesthetic value, the lack of distortion also makes it much easier for future adjustment to the design layout. Changes in scale and position of an object do not disrupt the visual projection of the entire scene, which accelerates the workflow to a great extent.
Both Adobe Illustrator and Cinema 4D (C4D) are commonly used for creating isometric designs. Compared to the process of scaling, sharing and rotating the shapes in Adobe Illustrator, the camera setting in C4D allows isometric projection rendered through the camera directly.

(2) Low-Poly modeling

3D models of lab instruments and research subject matters were created with a relatively small

number of polygons, to primarily reduce render time. Apart from working efficiency, models with low polygons can also have a desirable appearance. With compositions of basic geometry like cubes, cylinder, spheres and triangles, low-poly models offer a simple and clean aesthetic style, which is believed to be suitable in visualizing complex information.

User Interactive Experience: Scrolling

In computer displays, scrolling refers to sliding text, images or video across a monitor vertically or horizontally. "Scrolling" as a technique in user interactive development, does not change the layout of the text or imagery, but simply moves the user's view across the entire content. Users scroll down to reveal what is to be shown next and scroll up to review what has been displayed. This intuitive way of user interaction was incorporated in this thesis project to control the progress of the animated video, referring to a technique called "Scrolling Triggered Video Playback". The advantage and limitations of this technique are discussed below.

(1) Advantages of "Scrolling Triggered Video Playback"

Scrolling Triggered Video Site combines the advantages of traditional animation and web design. Users go through the website content as if they are watching a video. More importantly, they have full control over pacing based on how fast or slow they scroll.

The site supports a level of storytelling that cannot be accomplished with page-by-page navigation. With HTML5, Javascript, CSS3, and an animated video, a sophisticated story can be unfolded effectively using intuitive scrolling. "Scrolling up and down" controls "play", "pause" and "playback" of the video, which activates multi-plane animation, introduces new text and motion. This constant stimulation of changing elements instills a site with a film-like power that arouses curiosity, keeps users on-page and engaged longer. Additionally, the intuitive nature of scrolling-down prevents the audience from being overwhelmed by the navigation buttons, thereby promoting effective interactivity and guiding users to discover additional content.

Scrolling triggered Video Playback technique potentially presents a streamlined workflow in web development for both designers and web developers. In general, designers and web developers work in different ways to meet a variety of goals. Designers come up with designs of front-ends visual presentations and communicate the ideas with prototypes. Web developers then re-create the visual effects based on these prototypes using back-ends coding, allowing computers to calculate and respond to users' interactions. Scrolling Triggered Video Playback allows partial skip of this re-creating process. As long as the video is well designed and created, it can be displayed on an HTML canvas directly and controlled by pre-written JavaScript. Other functional elements, such as buttons or links can be added on to multiple HTML layers. The set of JavaScript, HTML and CSS documents provide a framework that can be reused for future development of a Scrolling Triggered Video sites. Any video can be placed and controlled using the same framework. This technique also makes future edits of the site much easier, which is particularly important for a public outreaching program. Changes to the design and content are required throughout the development and upon publication, based on user feedbacks and comments. These changes can be easily made in animation programs, such as Adobe After Effects to create a new version of the video. The old version could be easily replaced by changing the file name in JavaScript coding. No additional edits in HTML and CSS are needed.It is important to note that this scrolling feature functions differently on different browsers. Scrolling currently works on Safari, but appears choppy on Chrome. Further analysis and testing of the codes is ongoing.

(2) Potential limitations

First, with complex content, audiences might miss the big picture while scrolling down and going deeper to explore more detailed information. To avoid this problem, the site is composed of a main scrolling page that ends with a big picture and link to four sub-pages that provide more detailed information. Audiences can easily go back to the big picture wherever they are in the process. Additionally, special consideration was given to the navigation icons so users are

able to maintain a sense of where they are in the site and how much more to expect. Second, even though Scrolling site appears to be a popular trend in interactive design, it remains as a revolutionary user experience to some extent, compared to conventional "clicking". However, big brands like Nike, Sony and Apple have incorporated this into their web design as an eye-catching marketing tool that has proven to be very successful. I believe the communication of fundamental science could also benefit largely from this technique, as long as instructional graphic elements are clearly shown on the screen to guide the users.

Developing a Mechanism for Receiving Timely Feedback

Collecting timely feedback from actual users during and after the project development is essential for creating a public outreaching program. These feedbacks prove to be helpful in identifying potential problems, making adjustments, and measuring the success. Various ways of presenting ideas and receiving feedback were explored during the course of the project.

(1) Word Story combined with wireframes were firstly brought to the brain-storming sessions and follow-up meetings to show the framework of the program. Several versions of wireframe could be efficiently created for multiple rounds of feedback collection at initial stage of the project development.

(2) Animated prototype or animatics were shown to art advisor in the middle of the user interface design. Problems in visual presentations were directly exposed, including the timing and speed of the transitions, the amount of motions shown on the screen at the same time, and the effectiveness of using certain animations to explain the information.
Adobe After Effects (AE) and Keynote were used for creating the animated prototype. AE provides flexible and powerful functions to animate page transitions and motions. While creating animations in AE requires certain amount of time to test various parameter settings and keyframes. Keynote or MS Powerpoint, on the other hand, can be used to quickly test a rough

idea with the built-in animation presets. It is straight to the point — there is no code, timelines with keyframes or complicated functionality. Rapid and high-fidelity transitions and movements can be created and tested. The combination of the two programs were used to accelerate the workflow.

(3) Screen captures of the final user interface designs and rendered animations were shared with content and art advisors, as well as non-science viewers including family members and friends. Informal surveys were conducted to measure the effectiveness of the program. One major comment was that the original opening was probably too long, thus not strong enough. The story included in the opening was then replaced with one question "How does fundamental research help you?" to draw people's attention, since audience would probably show more interests in content that is directly relevant to their life.

(4) Contact forms will be included on the actual website. This allows long-term communication with the users. Future adjustment to the content and the design will be made according to their comments.

Appendix A: Informal Discussion List

From Fundamental Discovery to Human Health:

1.1 understanding basic science

- what is basic science
- what is basic science research
- why it is so important

1.2 Understanding research background

- what is Cell cytokinesis
- what is Cellular Mechanosensing
- how is cellular mechanosensing related to human health/ diseases

1.3 Understanding research concepts and process

a. experimental approach in model organisms:

- What are model organisms?
- Why are model organisms useful for fundamental research?
- How has work with research model organisms influenced human health?

b. from experimental to computational:

- what is computational modeling?
- How are computer models used to facilitate discovery?
- How can computational modeling improve biomedical research?
- Can computer models replace research organisms?

c. from theoretical models to human system:

- what are human-derived cells?
- how are human-derived cells important as vitro models in medicine?

- what do these cell lines tell us (in pancreatic cancer research)?

- what is immunohistochemistry?

- What information does immunohistochemistry provide to help understand human tissue?

d. from human system to therapeutic targets (compound screening):

- what is live cell high-throughput Screening?

- what have been discovered? (4-HAP treatment)

1.4 - Who funds basic research?

- How does basics research costs compared to total health care costs?

- What is the role of are basic research in improving health?

- Do we have evidence that research & development helps our economy?

Appendix B: Word Story

LANDING

How does fundamental research help you? (Scroll to explore)

INTRODUCTION

The population is aging, pathogens are spreading, and the demands on healthcare are increasing. Ebola, AIDS, and Influenza have dominated the headlines. Meanwhile, many of the complex diseases, like cancer, heart and lung disease, and diabetes, were once thought to be the "natural consequence of aging". However, these health problems result from the accumulated dysfunctions of cells and molecules. If scientists can uncover the basic mechanisms of these diseases, we will be able to solve them.

In the face of these health challenges, fundamental research has ventured into a world, filled with trillions of cells and molecules that make up the human body. In this highly dynamic world, cells grow, change shape, crawl, and contribute, sense and respond to environmental cues. Cellular molecules are constantly being made, moved, and modified. Although cells are constantly trying to get things right, sometimes mistakes are made.

Decades of fundamental studies are revealing clues about how these micro-level processes affect human health and how to repair them. Medical breakthroughs are made possible along the process. While many novel medicines, vaccines, and therapies have been developed, we are poised to expand our understanding of these cellular and molecular behaviors in order to create even better treatments.

Understand Fundamental Research

What is fundamental research after all?

Fundamental Research, or often called Basic science research, is a long-term process of studying living and non-living things in our environment, and inside OURSELVES, based on the

knowledge of basic sciences — physics, math, chemistry and biology.

The process we take part in is sophisticated and adventurous. Along this winding trail, we generate hypothesis, observe, test, measure, analyze and repeat.

(Keep Scrolling)

Understand the Complexity

Facing the unknown and uncertainties, we ask many basic questions: why cells move? how do they move? how do they communicate amongst themselves? All of these basic questions fall into three categories: (1) how do things function normally? (2) what would happen if the system breaks? (3) how to fix it?

Finding the answers to these basic questions, however, is greatly hindered by the extreme complexity of substantial molecules and cells of the human body. Direct experimental designs in human cells and tissues are not only difficult, but also time-consuming and economic-inefficient. To save time, money and materials, we have been seeking for simpler systems in which fundamental principles of biology and disease could be uncovered and defined.

Here we present a workflow, based on research projects carried out in the lab of Douglas Robinson in the department of Cell Biology at Johns Hopkins University School of Medicine.

The Robinson Lab studies cell mechanics, including mechano-responsive behavior of cells, and applies the concepts they are learning to developing novel therapeutics for complex diseases, such as cancer and chronic obstructive pulmonary diseases (COPD). (Click to read more)

RESEARCH STRATEGIES

01 SIMPLIFY

Human beings are very complex multicellular organisms (metazoans). A much simpler system is needed, in which experiments could be designed and carried out, fundamental principals of biology and disease can be uncovered and defined.

Luckily our cells contain the same fundamental materials as those of all living things.

Researchers can learn an abundance of knowledge about how our cells work by studying simpler organisms in lab settings. These organisms are called model organisms.

Simplify > Model organisms

Classic model organisms range from single-celled bacteria to more complex animals like mice. For example, *Escherichia coli* (E.coli) and viruses are great tools for genetic engineering and synthetic biology with their simple genomic composition and rapid growth rate. Fruit flies and honeybees and important research organisms for learning how genes and the environment interact to affect behavior. Zebrafish and worms can regrow missing or injured body parts, thus are used to learn how cells and tissues regenerate. Mice are commonly used to study disease development and test novel therapy.

Simplify > Model organisms > Dictyostelium

Dictyostelium discoideum (a.k.a. Dicty), a type of amoebozoan is a relatively recent addition to the list of model organisms for fundamental research. Dicty has proven to be a very effective tool in studying human cell behaviors. Living most of its life as a single, free-living amoeba consuming bacteria, its flexible plasma membrane without a rigid cell wall permits it to be highly motile, similar to human leukocytes. When it runs out of food, these free-living cells then join up and cooperate like an intelligent multicellular organism, forming many structures found in multicellular organisms such as epithelial tissues. Thus, these behaviors capture many of those presented by human cells and tissues. Moreover, the 34 Mb genome of Dicty contains many genes that are homologous to those in higher eukaryotes, including humans. These genes are either absent or are less accessible in other model organisms.

Addition to the behavior that capture a lot of attributes human cell have, Dicty also shows the common features of a model organism — can be rapidly grown to high cell densities in an inexpensive medium and easily observed under all forms of microscopy. Further, Dicty cells are easily studied biophysically. For mechanical studies, one common method is micropipette

aspiration (MPA). A small diameter glass pipet is brought into contact with the Dicty cell. A known suction pressure is then applied within the pipette, causing an aspiration of the cell into the pipette. By measuring the length of aspiration, several important cell mechanical properties, including cortical tension can be calculated. Cell deformability, in turn could be analyzed.

The combination of fluorescence microscopy and MPA enables high quality visualization of molecular components, including various proteins, during the process of cell shape change, as presented in the study of cell shape control at the Robinson Lab. Their studies in Dicty cells have revealed fundamental concepts. First, cell shape is maintained by a dynamic network of specific cytoskeletal proteins that interact tightly with the cell membrane. Second, within this network, a specific subset of cytoskeletal proteins sense and respond to mechanical stimuli and trigger subsequent cell shape change. This property is called mechanoresponsiveness, and these proteins are often referred to mechanoresponsive or mechanosensitive. These proteins are also critical components in cell movement and deformation, and are coordinated through a mechanical and biochemical feedback system. Third, if the expression of these proteins becomes abnormal, generally elevated, this leads to disrupted cell shape changes, movement, and mechanoresponsive. In cancer, this imbalance at protein level and migration at cell level could mutually reinforce each other to aggravate cancer metastasis.

02 PREDICT

Because of the considerable amount of sister proteins (or paralogs - proteins share the same origin) in human system that do not exist in Dicty cells (the Dicty genome is more streamlined), and the wide range of proteins in general, experimental results from these model organisms are still inconclusive in identifying the proteins that plays the role in human health and diseases. Computational Modeling, therefore, helps bridge the gap.

Predict > Computational Modeling

Computational Modeling is the use of math, physics and computer science to generate physical theories from experimental datasets. The power of computational modeling is that it allows scientists and engineers to simulate variations more efficiently by computer, saving time, money, and materials. The results of simulation help researchers make predictions about what will happen in the real system, most likely to develop further experimental design in human system.

Predict > Computational Modeling > Force-Dependent Model Predicts Mechanosensitivity

Myosins are a superfamily of motor proteins, well known for their roles in a wide range of cell motility processes. Studies in Dicty show that Myosin II is one of the mechanoresponsive proteins within the network of cytoskeleton, involved in cell shape maintenance and changes, as mentioned above. The three paralogs in human cells, namely Myosin IIA, IIB and IIC, were suspected to share the same property. Likewise, other mechanoresponsive proteins discovered in Dicty, such as alpha-actinin (ACTN) and Filamin, also have several sister proteins in human cells, which were also possibly to be utilized by cancer cells to achieve deformation and migration. In order to analyze the similarity and differences between these sister proteins in human cells and the homologous protein in Dicty, computer models were developed from experimental datasets generated from comprehensive investigation of Dicty, during which digital imaging, math, physics, and computer science were involved. The models allowed researchers to simulate the dynamics of sister proteins in human system. The statistical results of these simulations helped researchers predict several proteins attributes in human cells, such as mechanosensivity, reaction rate and localization patterns under different levels of mechanical stimulation. For instance, one of the simulation results suggested that under external mechanical stimulation, ACTN4 (one of the alpha-actinin paralogs) increased in intensity while ACTN1 did not, which indicated that ACTN4, but not ACTN1, was mechanoresponsive. The predictive power of the computational models greatly narrows the

range of molecular components to be tested in human cells and tissues, as well as the scope of the experimental design. These models, therefore, are very helpful tools in translating experimental results from model organisms to human systems.

03 TEST

With the guide of the computational predictions, experimental designs in human systems become more straightforward. Human derived cells and tissues were utilized at this point to test if the simulation correctly predicted the cell and protein behaviors.

Test > Human derived cells

Human derived cells are cells taken from human bodies, isolated and cultured in the laboratory under specific nutrients and space. Although they are removed from their normal context in human tissues, they still provide an invaluable tool for deciphering human disease relevant biology. Isolated cells allow for the examination of stepwise alterations in the structural and genetic makeup of the cell under controlled environments. However, many of these controlled environmental conditions include scenarios that reconstitute conditions the cells experience in normal tissue context. This ability to reconstitute defined tissue contexts with well-defined cells is especially valuable for studying complex tissues such as the pancreas, which is composed of various cell types and where in vivo examination of individual cells would be difficult. Further, the reconstituted tissue-like environments also allow for the ability to probe the cells and tissues, for example for mechanical studies.

Test > Human derived cells > Human Pancreatic Ductal Epithelial Cells & Pancreatic Adenocarcinoma-Derived Cells

In studies carried out in the Robinson Lab, several human-derived cells were investigated, to determine if the computational prediction of the mechanoresponsive property of the sister proteins in the human system is correct. These cell lines include immortalized Human Pancreatic Ductal Epithelial cells (HPDE), stage II pancreatic adenocarcinoma-derived cells

(Panc10.05), stage IV ascites-metastasis-derived cells (AsPC-1). HPDE cells are also used as a near normal pancreatic ductal epithelial cell comparator, while the others represent cancer cells in different disease states. In these cells, the targeted proteins were labeled with fluorescent proteins. Similar to the study of cell mechanics in Dicty, micropipette aspiration (MPA) was used to apply the external mechanical stimulation. The localization and concentration of the labelled proteins in response to applied external stress were measured. The experimental results were consistent with computational simulations, which confirmed the mechanoresponsive property of several previously suspected proteins, including Myosin IIC and ACTN4. The results also reflected the active involvement of these proteins in the process of cell shape change in both normal and cancer cells. Furthermore, cancer cells displayed higher level of cell deformation compared to the control group, as well as higher concentration of these proteins at the sites of deformation. This positive correlation between cell deformability and mechanoresponsive protein level in human derived cells highly suggested that mechanoresponsive proteins might be harnessed by cancer cells, leading to altered cell shape control and cell motility.

Test > Human Tissue

Patients' tissues are samples taken directly from patients during surgical resection to remove the patient's tumors (with patient consent). These samples provide direct information about disease states and are used to test whether discoveries in model organisms and human-derived cells are consistent with real-life situations.

Test > Human Tissue > PDAC Tissue Sample

To test if these mechanosensory proteins, such as Myosin IIC, were over produced in pancreatic cancer, tissue samples from PDAC patients were collected. Testing was achieved by using immunohistochemistry (antigen-antibody and tissue-based reaction), a method of tissue imaging. Secondary antibodies coupled with horse radish peroxidase (HRP) were applied

to the tissue slides followed by the chromagen DAB with which the HRP reacts to create a brown color. Where the tissue turns brown reflects where the protein is found, and protein concentration is represented by the intensity of the pigments. The resulting images observed under light microscope indicate that Myosin IIC and other mechanosensory proteins were highly up-regulated in the pancreatic ductal adenocarcinoma of patients, compared to normal tissues. The level of up-regulation is positively correlated to the stage of pancreatic cancer, further confirming that these mechanosensory proteins are critical components of cancer cell shape change and migration. Hence, these proteins might be potential therapeutic targets in reducing cancer metastasis.

04 SCREEN

The experimental results from both model and human systems suggest that one rational therapeutic approach is to correct tumor cell behavior by reducing cell deformation (in other word, increasing cell stiffness), which would in turn, reduce metastatic potential of cancer. This could be achieved by interfering with the mechanosensitive proteins like Myosin IIC, using small-modulators (small compounds).

Screen > High-Throughput Chemical Screening System

To seek for effective small compounds, an in vivo, high-throughput, chemical screening system was developed. This system enables the efficient discovery of possible drug precursors. Large numbers of compounds from compound libraries were added to and interact with cells in thousands of reacting wells. Sensitive detectors and data processing software made it possible to accurately pick up these potential compounds based on their ability to inhibit cell shape change

Screen > High-Throughput Chemical Screening System > 4-HAP

A small compound, 4-hydroxyacetophenone (4-HAP) was characterized by the Robinson Lab during the screening process. 4-HAP reduces cell deformation by forcing Myosin II to re-localize

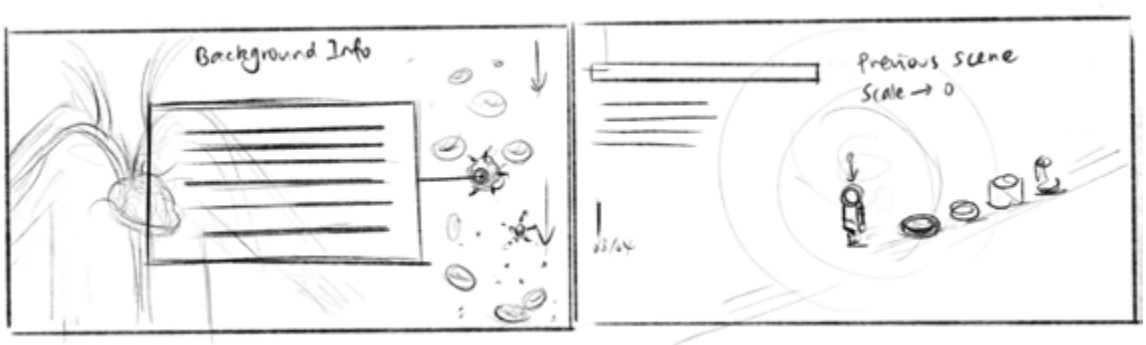
along the cell skin (cell cortex). Such re-localization of mechanosensitive proteins increases cellular cortical tension and subsequent cell stiffness. In a mouse liver metastasis model, 4-HAP treatment reduced the metastasis of pancreatic tumors to liver, in comparison with the control group.

UNFINISHED AGENDA

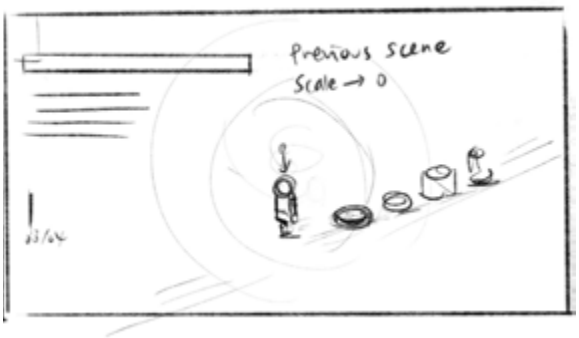
(The story is to be continued ...)

Appendix C | Storyboards

<Motion Design 1-2 > Loading page is composed of a moving amoeba at the center and a progress percentage underneath. The landing page shows a loop animation at the center of the screen, showing Bunsen Burner, petri dishes, and a flask (items that viewers are familiar with and can relate to basic research) A question "How does fundamental research help you?" will be typed on the screen (motion graphics). "Fundamental Research" and "YOU" will be highlighted to build the connection with viewers. The animated icon "Scroll to explore" shows up at this point to provide instruction. Not all text included in the image is intended to be read.



<Motion Design 3-4 > Main page is reached by scrolling. Background animation shows human circulation system, red blood cells and foreign pathogens to represent current health problems. As viewers scrolls and finish reading the paragraph, scene 1 scales down to zero and drops "into" the researcher's head. Scene 2 is composed of a researcher, a flask, and petri dishes with bacteria colonies, slime mold and amoebazoan cells. Models are placed along the isometric grids. Text shows up at the top left corner. Now the researcher has guided viewers to"venture into the world of fundamental research. Not all text included in the image is intended to be read.



<Motion Design 5> Then a set of models representing "medical and technological" breakthrough enters the screen and bumps the "lab items" to the left. The researcher stays at the same position. Animated arcs indicate the relationship between research and medicine. This is the end of the introduction part 1, which generally states the fact that we depend on fundamental research to face health challenges. As viewers scroll, the scroll bar shows the progress. Not all text included in the image is intended to be read.

<Motion Design 6-7 > Page number changes to 02. Previous models build out along the isometric axis. The researcher stays. A new set of models build in along the same axis, displaying a broader set of items involved in basic sciences while introducing "what is fundamental research?". Models to be reused in the next scene are positioned at the center. The rest of the models leave the screen along the isometric axis, meanwhile slightly enlarging the models stay on the screen. Animated arcs indicate the research process. This is the end of the introduction part 2. Not all text included in the image is intended to be read.

<Motion Design 8 > Introduction section 2 are scrolled up immediately followed by section 3. Researcher and one capsule show up at the center of the screen. A circle appears in the motion of "trim path" behind the capsule where the animation of "cancer cell movement" are shown. Three question mark appears on top of the researcher's head, indicating that "before we can cure diseases, researchers need to find answers to many questions", and that the all of these basic questions fall into three categories. Scrolling controls the highlighting of each question as well as the progress of the animations that represent the question. The animations are masked by the circle. Not all text included in the image is intended to be read.

<Motion Design 9> The same pattern is used for the last page of this section. As the new section "Strategy" is introduced to the screen. The circle with animation playing inside split into 2, 3 and 4, representing "Simplify", "Test", "Predict", and "Screen", with the effect of "simple choker" and " fast blur" in AE. This is the last scene of the Introduction page. Users can click into each title to read more. Not all text included in the image is intended to be read.

<Motion Design 10> Long horizontal scrolling page is designed for the content page. The body paragraph is presented at the center with the 3D models and images show up at the lower 1/3 of the screen. As users scroll, the imagery move horizontally. Text transitions are achieved by the change of opacity. Not all text included in the image is intended to be read.

<Motion Design 11> Scrolling up the main page reveals the stick footer. T**he** footer is composed of contact information, contact form and a map. Not all text included in the image is intended to be read.

Appendix D: HTML (JavaScripts Incorporated)

```
<html>
<head>

    <title> How Does Fundamental Research Help You </title>

    <link href="FundamentalResearchHelpYou.css" rel="stylesheet" type="text/css" />

   <script src="particle_sdl.js"></script> // optional HTML canvas animation

</head>
 <body>

 <div id="Arena">

        <div id="Container">

            <img id="preface" src="opening.gif"></img> // opening animation

            <video id="Content" loop>

            <source type="video/webm;" src="animatics_whole.webm"></source>

            <source type="video/mp4;" src="animatics_whole.mp4"></source>

            <source type="video/ogg;" src="animatics_whole.ogv"></source>

            <p>Sorry, your browser does not support the &lt;video&gt; element.</p>

            </video>
        </div>

        <audio id="ArenaAudio" src="bg_music.mp3" loop></audio>

        <canvas id="ArenaCanvas"> </canvas>

        <div id="ContactForm">

            <form method="post" action="server.php">

            <p><label>name: <input name="username" type="text" placeholder="please input
 name"></label></P>

            <p><label>e-mail: <input name="mailaddr" type="text"></label></P>

            <p><label>message: <input name="message" type="text"></label></P>

            <p><button>send me</button></p>

            </form>

        </div>
```

```
<div id="Afterword"> // sticky footer
        <div id="awContact">
            <div id="awContactImg1"> // contact info
                <img id="AfterwordImg1" src="mtxx20180308_1.png"></img>
            </div>
            <div id="awContactImg2">
                <img id="AfterwordImg2" src="mtxx20180308_2.png"></img>
            </div>

            <div id="awContactForm"> // Contact form
                <p class="awTitle">CONTACT ME</p>
                <ul class="email">
                <li><input type="text" name="name" placeholder="Name"></li>
                <li><input type="text" name="email" placeholder="Email Address"></li>
                <li><input type="text" name="number" placeholder="Phone Number"></li>
                <li class="message"><textarea name="message" placeholder="Message"></textarea>
</li>
                 <button class="btn-define">Submit</button>
                 <a href="mailto" id="send"></a>
                 </ul>
                </p>
              </div>

              <div id="awContactImg2"> // map
                <img id="AfterwordImg3" src="mtxx20180308_3.png"></img>
              </div>
          </div>
</div>
```

```
<script type="text/JavaScript">

 // get HTML ID

 var arenaDiv = document.getElementById("Arena");

 var prefaceImg = document.getElementById("preface");

 var ContentVideo = document.getElementById("Content");

 var arenaAudio = document.getElementById("ArenaAudio");

 var arenaCanvas = document.getElementById("ArenaCanvas");

 var contactForm = document.getElementById("ContactForm");

// Hide video and footer information

ContentVideo.style.visibility = "hidden";

contactForm.style.visibility = "hidden";

 // Variation Initialization

 var arenaScale = 500; // how much to play when scrolling once

 var videoTimerID = 0;  // videoPlay timer

 var canvasTimerID = 0; // background animation Timer

 var part = CreateParticle (3, "ArenaCanvas"); // background animation, support 3 styles


//load document, main event handler function

 document.onreadystatechange = function() {


//once the video/document finishes loading, get video duration, set scrolling depth;

    if(document.readyState == "complete") {

    totalDuration = ContentVideo.duration;

     arenaDiv.style.height = Math.floor(totalDuration) * arenaScale + "px"; // set unit to "px"
```

```
    //set canvas timer for background animation, loop every 40 seconds;
     canvasTimerID = window.setInterval(function(){part.drawDots();}, 40);
   //play background music
   arenaAudio.play();
  }
// get document height
function getDocumentTop() {
      var scrollTop = 0, bodyScrollTop = 0, documentScrollTop = 0; // different browsers
      if(document.body) {
            bodyScrollTop = document.body.scrollTop;
            }
      if(document.documentElement) {
            documentScrollTop = document.documentElement.scrollTop;
            }
      // console.log("==="+bodyScrollTop+"|"+documentScrollTop);
      scrollTop = (bodyScrollTop - documentScrollTop > 0) ? bodyScrollTop :  documentScrollTop;
      return scrollTop; // return the bigger value
}
// get window height
   function getWindowHeight() {
         var windowHeight = 0;
         if(document.compatMode == "CSS1Compat") {
               windowHeight = document.documentElement.clientHeight;
         } else {
               windowHeight = document.body.clientHeight;
               }
         return windowHeight;
      }
```

```
// get scroll bar height
function getScrollHeight() {
    var scrollHeight = 0, bodyScrollHeight = 0, documentScrollHeight = 0;
    if(document.body) {
        bodyScrollHeight = document.body.scrollHeight;
        }
    if(document.documentElement) {
        documentScrollHeight = document.documentElement.scrollHeight;
        }
    scrollHeight = (bodyScrollHeight - documentScrollHeight > 0) ? bodyScrollHeight :
documentScrollHeight;
    return scrollHeight;
}

// Scrolling event-handler
window.onscroll = function() {
  closeTimer();
  var s_Top = getDocumentTop();
  var s_Height = getScrollHeight();
  var w_Height = getWindowHeight();
  if(s_Top == 0) {
    showOnTop();
  } else if(s_Height == s_Top + w_Height) {
    showOnBottom();
  } else {
    showScroll();
}
```

```
// play video when scrolling
    function scrollPlay() {
        ContentVideo.currentTime = window.pageYOffset/arenaScale;
        videoTimerID = window.requestAnimationFrame(scrollPlay); // update calculation
    }
// Scrolling event function1: regular scroll
    function showScroll() {
    if(prefaceImg.style.visibility !== "hidden") prefaceImg.style.visibility = "hidden";
    if(ContentVideo.style.visibility !== "visible") ContentVideo.style.visibility = "visible";
    if(arenaCanvas.style.visibility !== "hidden") arenaCanvas.style.visibility = "hidden";
    if(contactForm.style.visibility !== "hidden") contactForm.style.visibility = "hidden";
    ContentVideo.style.opacity = 1.0;
    ContentVideo.pause();
    arenaAudio.pause();
    scrollPlay();
  }
//Scrolling event function2: go back to the top and autoplay video
    function showOnTop() {
    if(prefaceImg.style.visibility !== "hidden") prefaceImg.style.visibility = "hidden";
    if(ContentVideo.style.visibility !== "visible") ContentVideo.style.visibility = "visible";
    if(arenaCanvas.style.visibility !== "visible") arenaCanvas.style.visibility = "visible";
    if(contactForm.style.visibility !== "hidden") contactForm.style.visibility = "hidden";
    ContentVideo.style.opacity = 1;
    ContentVideo.play();
    arenaAudio.play();
    if(canvasTimerID == 0) {
        canvasTimerID = window.setInterval(function(){part.drawDots();}, 40);
        }
}
```

```
    function showOnBottom() {
        if(prefaceImg.style.visibility !== "hidden") prefaceImg.style.visibility = "hidden";
        if(ContentVideo.style.visibility !== "hidden") ContentVideo.style.visibility = "hidden";
        if(arenaCanvas.style.visibility !== "hidden") arenaCanvas.style.visibility = "hidden";
        if(contactForm.style.visibility !== "visible") contactForm.style.visibility = "visible";
    }


    // close Timer, cancel animation
    function closeTimer() {
        if(canvasTimerID > 0) {
        window.clearInterval(canvasTimerID);
        canvasTimerID = 0;
        };

        if(videoTimerID > 0) {
        window.cancelAnimationFrame(videoTimerID);
        videoTimerID = 0;
        };
     }


};


    </script>
</body>
</html>
```

Appendix E: CSS

```
#Arena {
   display: block;
}

#Container {
   position: fixed;
   left: 0;
   top: 0;
   width: 100%;
   height: 100%;
}

#preface {
   position: fixed;
   left: 0;
   top: 0;
   width: 100%;
   height: 100%;
   opacity: 0.5;
   bject-fit: fill; /*fill | contain | cover | none | scale-down */
}

#Content {
   position: fixed;
   left: 0;
   top: 0;
   width: 100%;
   height: 100%;
   z-index: -100;
   opacity: 1.0;
   object-fit: fill; /*fill | contain | cover | none | scale-down */
}
```

```
#ArenaCanvas {
position: fixed;
min-width: 100%;
min-height: 100%;
width: auto;
height: auto;
color: “#555”;
background-color: “#000”;
z-index: 100;
}

#Afterword {
width: 100%;
opacity: 1.0;
}

#awText {
width: 100%;
background-color: #DCDCDC;
z-index: 100;
}

#awContact {
position: fixed;
bottom: 0;
width: 100%;
background-color: #DCDCDC;
z-index: -100;
}

#awContactImg1 {
position: relative;
width: 100%;
}
```

```
#awContactImg1 img {
min-width: 100%;
}

#awContactImg1 button {
position: absolute;
right: 10; top: 10;
z-index: 50;
}

#awContactImg2 {
width: 30%; height: 200px;
float: left;
}

#awContactImg2 img {
object-fit: fill; /*fill | contain | cover | none | scale-down */
}

#awContactForm {
width: 30%; height: 200px;
float: left;
/*display:inline-block;*/
}

#awContactImg3 {
width: 40%; height: 200px;
float: left;
}

#awContactImg3 img {
max-width: 100%; min-width: 100%;
object-fit: fill; /*fill | contain | cover | none | scale-down */
}

p font-family DINPro {
   font-size: 24px;
}
```

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VITA

Tianxing "Mary" Shi was born in Beijing, China. Grew up in a family of researchers, Mary was exposed to science at an early age and showed great interest in chemistry and biology since middle school, which has always been encouraged by her parents.

Mary continued to pursue biology at the University of Hong Kong of Science and Technology. During her time in college, she worked as a research student in the marine natural product lab and as an chief art editor for the student editorial. In the June of 2014, she received an Honored Bachelor of Science in Biology. Upon graduation, Mary continued to work in cellular and molecular field as a full time graduate research fellow in the University of Hong Kong, Li Ka Shing Faculty of Medicine.

Years of reading research papers and design magazines, has largely inspired her creative and critical thinking and made her realize the essential role of visualization in explaining complex information. These experiences peaked her interest in attending the graduate program of Medical and Biological Illustration at Johns Hopkins School of Medicine, Department of Art as Applied to Medicine where she currently attends. The curriculum has challenged her to use her science background, research experience, artistic skills and design sense to clearly express scientific and medical information to a wide variety of audiences.

During her first year of graduate study she was awarded the Association of Medical Illustrators Award of Excellence in the animation category. She is currently a candidate to receive a Master of Arts on May 23, 2018.

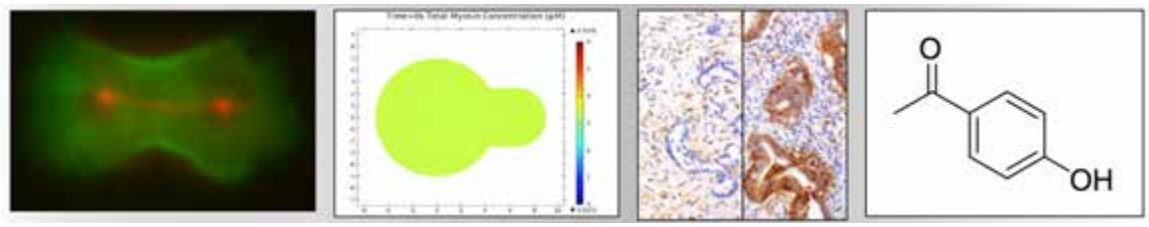

Figure 1. A workflow from fundamentals to therapeutic targets. The workflow is generalized into a series of four methods: Simplify (Model system), Predict (Computational modeling), Test (Human system) and Screen (High-throughput chemical screening). Text included in the image is not intended to be read.

(1) **Simplify: Model system**

Human beings are very complex multicellular organisms. But our cells contain the same fundamental materials as those of all living organisms. Researchers, therefore, can learn an abundance of knowledge about how our bodies work by studying simpler organisms, often called model organisms, in the lab setting.

In these model organisms, experiments can be designed and carried out to define fundamental principles of biology and disease. Common features of model organisms include rapid growth to high cell densities in an inexpensive medium, as well as accessible means of observation and manipulation. Classic model organisms range from single-celled bacteria to more complex animals such as mice. For example, the bacteria *Escherichia coli* (E. coli) is an excellent tool for genetic engineering and synthetic biology; fruit flies and honeybees are important model organisms for learning about how genes and the environment interact to affect behavior; worms and zebrafish can regrow missing or injured body parts, thus are used to learn about how cells and tissues regenerate. Mice are commonly used to study disease development and test novel therapies including drugs and vaccines (NIGMS, 2011).

Dictyostelium discoideum (a.k.a. Dicty) (**Fig. 2**), a type of amoebozoan is a relatively recent addition to the list of model organisms for fundamental research. Dicty has proven to be a very effective tool in studying human cell behaviors. Living most of its life as a single, free-living amoeba consuming bacteria, its flexible plasma membrane without a rigid cell wall permits it to be highly motile, similar to human leukocytes. When it runs out of food, these free-living cells

then join up and cooperate like an intelligent multicellular organism, forming many structures found in multicellular organisms such as epithelial tissues. Thus, these behaviors capture many of those presented by human cells and tissues. Moreover, the 34 Mb genome of Dicty contains many genes that are homologous to those in higher eukaryotes, including humans (DictyBase, 2010). These genes are either absent or are less accessible in other model organisms.

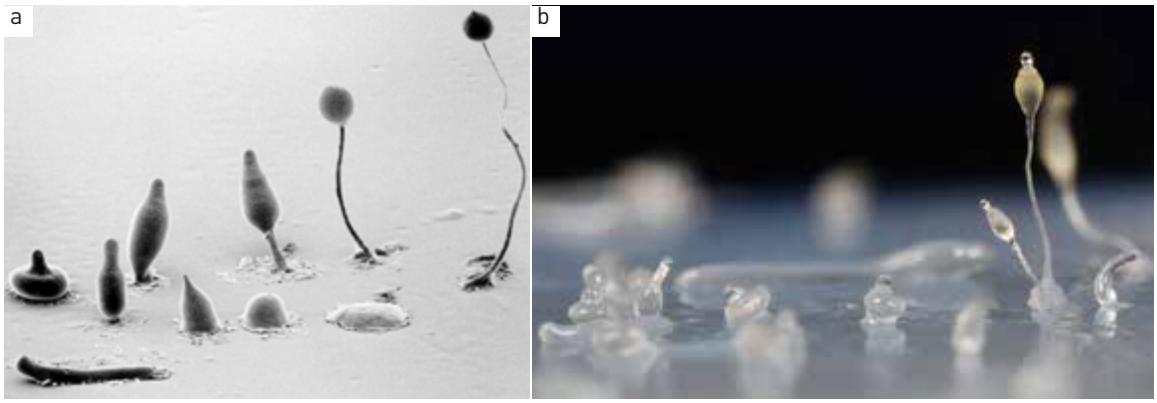

Figure 2a. SEM of *Dictyostelium discoideum* (Dicty) developmental stages. Copyright M.J. Grimson & R.L. Blanton; Biological Sciences Electron Microscopy Laboratory, Texas Tech University. **2b. The beauty of *Dictyostelium discoideum* under stereoscope.**

Many phases of health and disease depend on the behaviors of individual cells that are clearly displayed in Dicty. For example, cytokinesis, a process easily observed in Dicty, is critical in understanding cell proliferation and is therefore an integral part of immune response, tissue maintenance, and cancer development. Further, as a model shape change process, cytokinesis captures most of the critical features, including the biochemistry and mechanics of cell shape change events more broadly. Cell motility, a characteristic feature of Dicty, is an essential early event in the metastasis of tumor cells and in angiogenesis by endothelial cells. Chemotaxis and phagocytosis are prominent features of Dicty, which are powerful for studying mechanisms behind inflammation, asthma, immune surveillance and antigen presentation (DictyBase, 2010). More importantly, Dicty is uncomplicated to handle in lab settings. The size of Dicty is the same size as a human leukocyte and can be easily observed under light microscope. Fluorescence

labeling further enhances the presentation of its cellular components (**Fig. 3**), and Dicty are particularly amenable to genetic manipulation. Further, Dicty cells are easily studied biophysically. For mechanical studies, one common method is micropipette aspiration (MPA) (**Fig. 4**). In this technique, a small diameter glass pipette is brought into contact with the Dicty cell. A known suction pressure is then applied within the pipette, causing an aspiration of the cell into the pipette. By measuring the length of aspiration, several important cell mechanical properties, such as cortical tension, can be calculated. Cell deformability, in turn, could be analyzed. The combination of fluorescence microscopy and micropipette aspiration (**Fig. 5**) enables high quality visualization of molecular components, including various proteins, during the process of cell shape change, as presented in the study of cell shape control at the Robinson Lab. Their studies in Dicty cells have revealed several fundamental concepts:

(1) Cell shape is maintained by a dynamic network of specific cytoskeletal proteins that interact tightly with the cell membrane.

(2) Within this network, a specific subset of cytoskeletal proteins sense and respond to mechanical stimuli and trigger subsequent cell shape change. This property is called mechanoresponsiveness, and these proteins are often referred to mechanoresponsive or mechanosensitive. These proteins are also critical components in cell movement and deformation, and are coordinated through a mechanical and biochemical feedback system.

(3) If the expression of these proteins becomes abnormal, generally elevated, this leads to disrupted cell shape changes, movement, and mechanoresponsive. In cancer, this imbalance at protein level and migration at cell level could mutually reinforce each other to aggravate cancer metastasis.

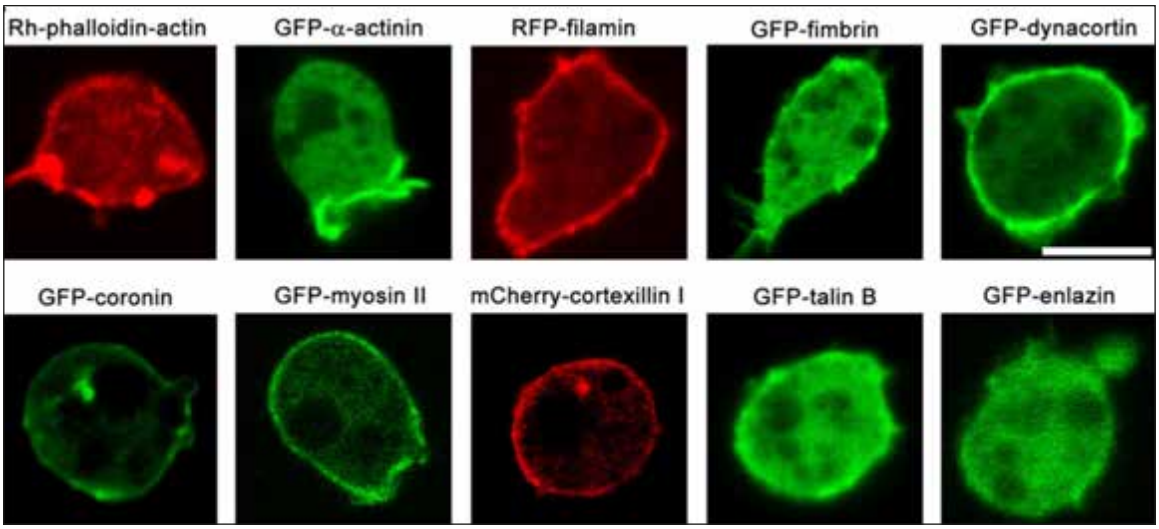

Figure 3. Fluorescence labeling showing the distribution of cytoskeletal proteins in different mutants of Dictyostelium under confocal microscopy (Luo et al. 2013).

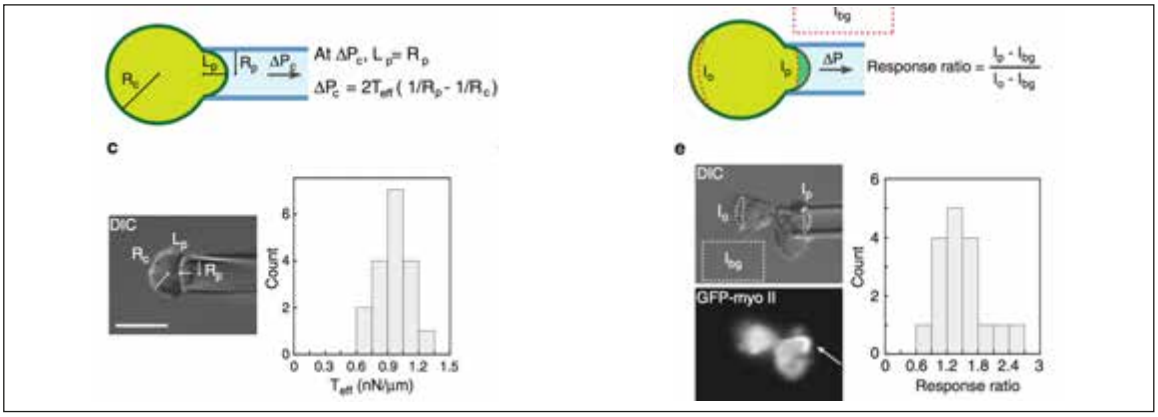

Figure 4. Manipulation of cells by Micropipette Aspiration for cortical tension and mechanosensitivity analysis (Kee and Robinson. 2013). Text not intended to be read.

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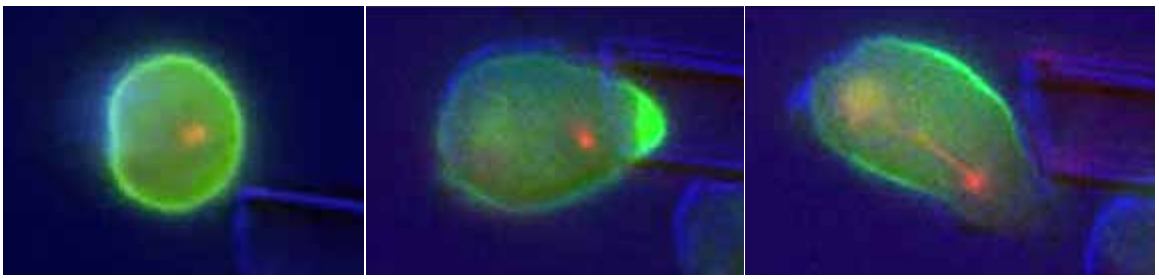


Figure 5.Manipulation of Dicty cells by fluorescence labelling and micropipette aspiration for studying cell shape control (Effler et al. 2006; Ren et al. 2009; Kee et al. 2012).

(2) Predict: Computational modeling

Because of the considerable amount of sister proteins (or paralogs - proteins share the same origin) in human system that do not exist in Dicty cells (the Dicty genome is more streamlined), and due to the wide range of proteins in general, experimental results from these model organisms are still inconclusive in identifying the proteins that plays the role in human health and diseases. Computational Modeling, therefore, helps bridge the gap.

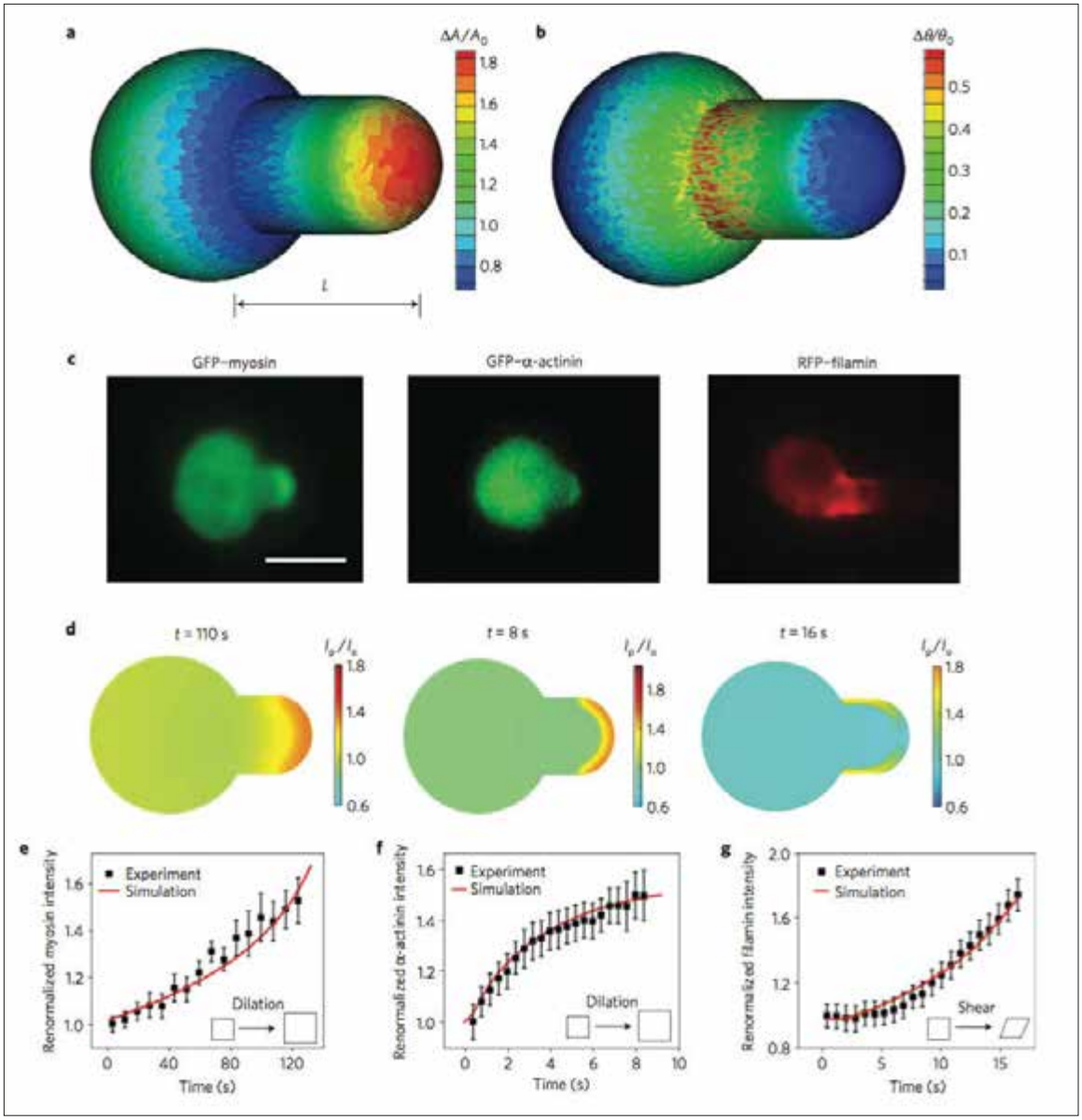


Figure 6. Example of computational modeling. Digital imaging and kinetic simulations were included in the process (Luo et al. 2013). Text not intended to be read.

Myosins are a superfamily of motor proteins, well known for their roles in a wide range of cell motility processes. Studies in Dicty show that Myosin II is one of the mechanoresponsive proteins within the network of cytoskeleton, involved in cell shape maintenance and changes, as mentioned above. The three paralogs in human cells, namely Myosin IIA, IIB and IIC, were suspected to share the same property. Likewise, other mechanoresponsive proteins discovered in Dicty, such as alpha-actinin (ACTN) and Filamin, also have several sister proteins in human cells, which were also possibly to be utilized by cancer cells to achieve metastasis.

To analyze the similarity and differences between these sister proteins in human cells and the homologous protein in Dicty, computer models were developed and utilized. To develop the computer models, and the underlying physical theories, experimental datasets generated from comprehensive investigation of Dicty were collected and analyzed, during which digital imaging, math, physics, and computer science were involved (**Fig. 6**). The theories allowed researchers to simulate the dynamics of sister proteins in the human system. The statistical results of these simulations helped researchers predict several protein attributes in human cells, such as mechanosensivity, reaction rate and localization patterns under different levels of mechanical stimulation. For instance, one of the simulation results (**Fig. 7**) suggested that under external mechanical stimulation, ACTN4 (one of the alpha-actinin paralogs) increased in intensity while

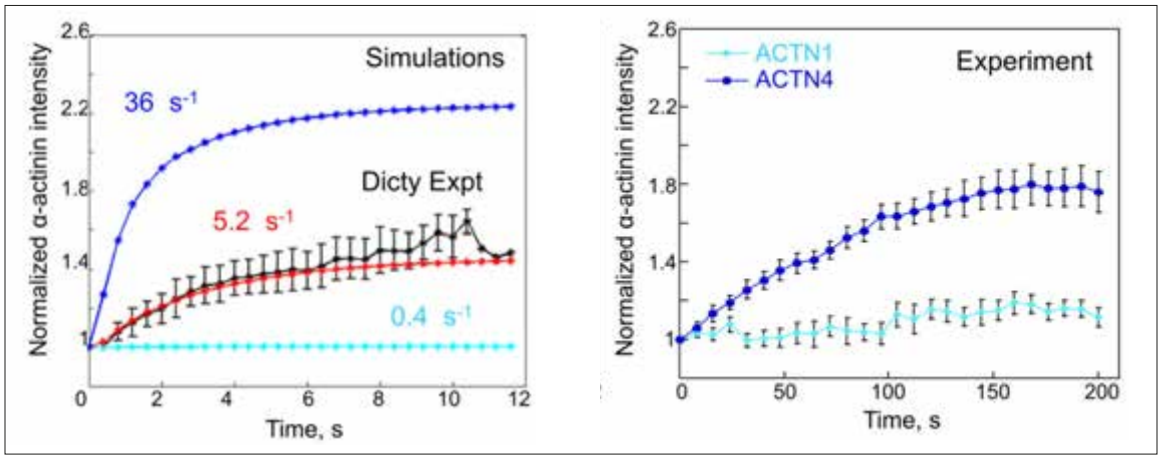


Figure 7. A force-dependent model based on Actin-binding affinity predicts the mechanoaccumulative behavior of α-Actinin sister proteins (Schiffhauer el al. 2016).

ACTN1 did not, indicating that ACTN4 but not ACTN1, was mechanoresponsive.

The predictive power of the computational models decreases the range of molecular components to be tested in human cells and tissues, as well as decreases the scope of the experimental design. These models, therefore, are very helpful tools in translating experimental results from model organisms to human systems. Moreover, computational modeling allows scientists to simulate variations rather efficiently, saving considerable time, money, and materials.

(3) Test in human system

With the guide of the computational predictions, experimental designs in human systems become straightforward. Human derived cells and tissues were utilized at this point to test if the simulation correctly predicted the cell and protein behaviors.

Human derived cells are cells taken from human bodies, isolated and cultured in the laboratory under specific nutrients and space. Although they are removed from their normal context in human tissues, they still provide an invaluable tool for deciphering human disease relevant biology. Isolated cells allow for the examination of stepwise alterations in the structural and genetic makeup of the cell under controlled environments. However, many of these controlled environmental conditions include scenarios that reconstitute conditions the cells experience in normal tissue context. This ability to reconstitute defined tissue contexts with well-defined cells is especially valuable for studying complex tissues such as the pancreas, which is composed of various cell types and where in vivo examination of individual cells would be difficult. Further, the reconstituted tissue-like environments also allow for the ability to probe the cells and tissues, for example for mechanical studies.

In the studies carried out in the Robinson Lab, several human-derived cells were investigated, to determine if the computational prediction of the mechanoresponsive property of the sister proteins in the human system is correct. These cell lines include immortalized Human Pancreatic Ductal Epithelial cells (HPDE), stage II pancreatic adenocarcinoma-derived cells

(Panc10.05), stage IV ascites-metastasis-derived cells (AsPC-1). HPDE cells are also used as a near normal pancreatic ductal epithelial cell comparator, while the others represent cancer cells in different disease states. In these cells, the targeted proteins were labeled with fluorescent proteins. Similar to the study of cell mechanics in Dicty, micropipette aspiration (MPA) was used to apply the external mechanical stimulation. The localization and concentration of the labelled proteins in response to applied external stress were observed and measured. The experimental results (**Fig. 8**) were consistent with computational simulations, which confirmed the mechanoresponsive property of several previously suspected proteins, including Myosin IIC and ACTN4. The results also reflected the active involvement of these proteins in the process of cell shape change in both normal and cancer cells. Furthermore, cancer cells displayed higher levels of cell deformation compared to the control group, as well as higher concentration of these proteins at the sites of deformation. This positive correlation between cell deformability and mechanoresponsive protein level in human derived cells highly suggested that mechanoresponsive proteins might be harnessed by cancer cells, leading to altered cell shape control and cell motility.

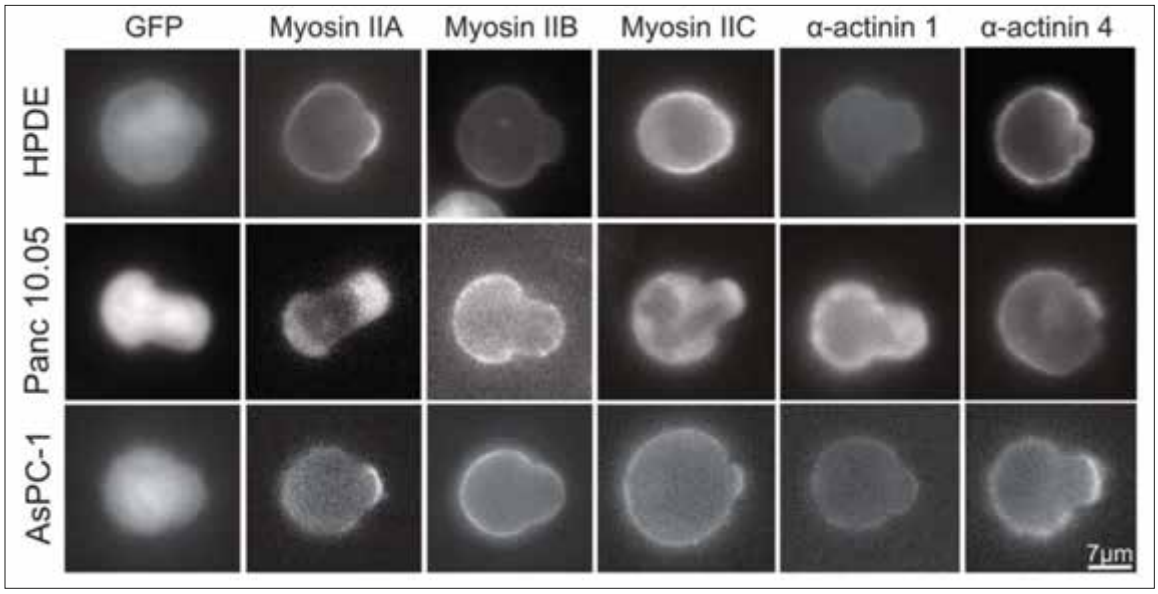


Figure 8. Representative images across multiple human derived cell lines show peak intensity after applied stress in MPA mechanoresponse experiments (Surcel el al, 2017).

This correlation between cell shape change and protein dynamics was then further tested in patients' tissue samples isolated directly during surgical resection to remove the patient's tumors (with patient consent). These samples provide direct information about disease states and are used to test whether discoveries in model organisms and human-derived cells are consistent with real-life situations.

To test if these mechanosensory proteins, such as Myosin IIC, were over produced in pancreatic cancer, tissue samples from PDAC patients were collected. Testing was achieved by using immunohistochemistry (antigen-antibody and tissue-based reaction), a method of tissue imaging. Secondary antibodies coupled with horse radish peroxidase (HRP) were applied to the tissue slides followed by the chromagen DAB with which the HRP reacts to create a brown color. Where the tissue turns brown reflects where the protein is found, and protein concentration is represented by the intensity of the pigments. The resulting images observed under light microscope indicate that Myosin IIC and other mechanosensory proteins were highly up-regulated in the pancreatic ductal adenocarcinoma of patients, compared to normal tissues (**Fig. 9**). The level of up-regulation is positively correlated to the stage of pancreatic cancer, further confirming that these mechanosensory proteins are critical components of cancer cell

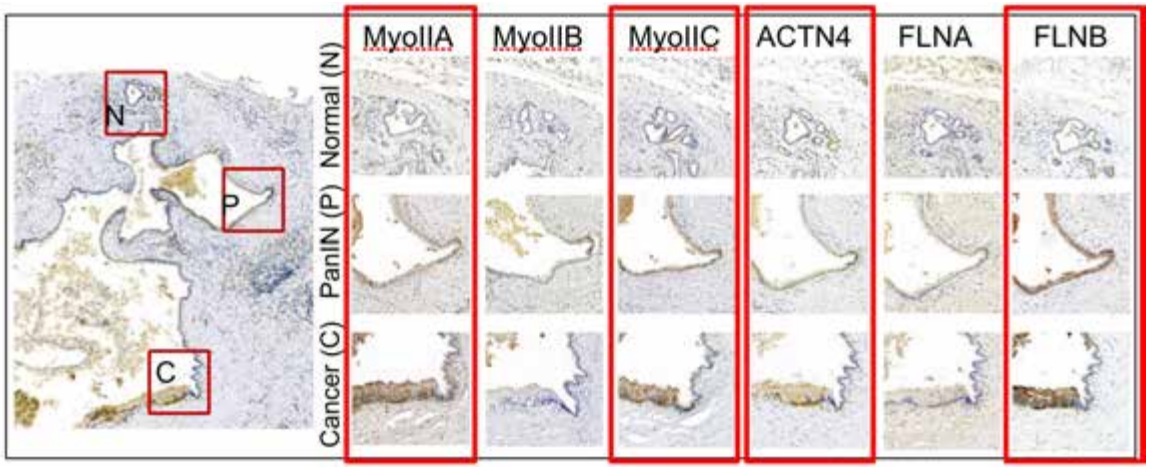


Figure 9. The mechanoresponsive machinery is elevated in pancreatic ductal adenocarcinoma in human pancreatic tissue (Surcel el al, 2017).

shape change and migration. Hence, these proteins might be potential therapeutic targets in reducing cancer metastasis.

(4) Screening: High-throughput chemical screening system

The experimental results from both model and human systems suggest that one rational therapeutic approach is to correct tumor cell behavior by reducing cell deformation (in other word, increasing cell stiffness), which would in turn, reduce metastatic potential of cancer. This could be achieved by interfering with the mechanosensitive proteins like Myosin IIC, using small-modulators (small compounds).

To seek for effective small compounds, an in vivo, high-throughput, chemical screening system was developed. This system enables the efficient discovery of possible drug precursors. Large numbers of compounds from compound libraries were added to and interact with cells in thousands of reacting wells. Sensitive detectors and data processing software made it possible to accurately pick up these potential compounds based on their ability to inhibit cell shape change. A small compound, 4-hydroxyacetophenone (4-HAP) was characterized by the Robinson Lab. 4-HAP reduces cell deformation by forcing Myosin II to re-localize along the cell cortex. Such re-localization of mechanosensitive proteins increases cellular cortical tension and subsequent cell stiffness. In a mouse liver metastasis model, 4-HAP treatment (**Fig. 10**) reduced the metastasis of pancreatic tumors to liver, in comparison with the control (Surcel el al, 2017).

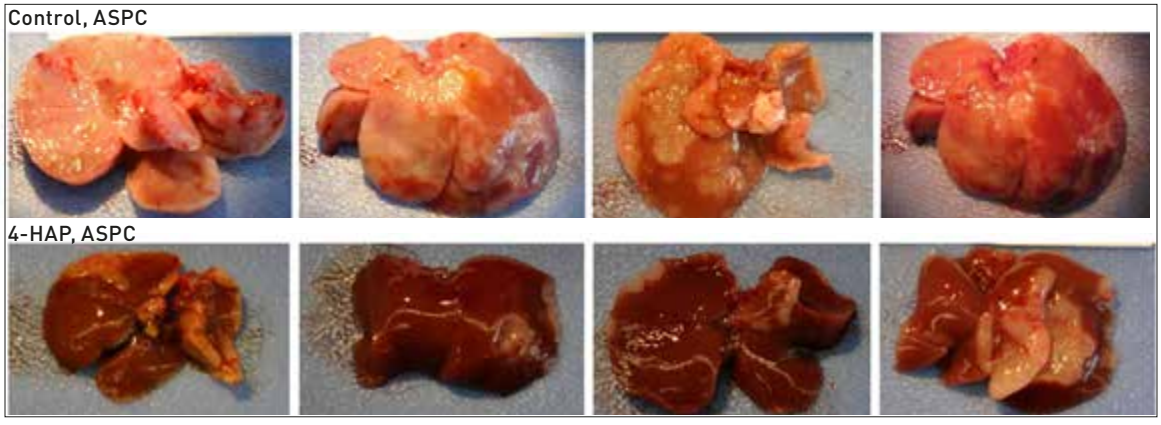


Figure 10. 4-HAP treatment in a murine model of metastatic pancreatic cancer (Surcel el al, 2017).

Objectives

This project explores the effectiveness of employing a combination of visual elements, including 3D models and animations, 2D motion graphics and interactive designs, for making an engaging and successful public outreach piece. The final product will be presented in the form of an interactive website, intended to provide a broad overview of fundamental research to the general public in an aesthetic and easy to navigate format.

The content will be divided into the following three sections:
(1) Landing Page – To draw attention and inspires further consideration.
(2) Introduction Page - To provide background information on fundamental research.
(3) Research Strategies – To explain why scientists do what they do in the context of the study of cell shape control in cancer treatment (specifically from the Robinson Lab at Johns Hopkins School of Medicine).

Audience

The primary audience will be composed of members of the lay public including potential funders and policy makers who may not have a science background. The appreciation of the importance and relevance of fundamental science is critical in gaining the appropriate support for biomedical research that leads to better healthcare. The secondary audiences are scientists and bio-communicators who are interested in public outreach about fundamental research.

MATERIALS AND METHODS

Literature Review

Literature and web reviews were initially conducted on the following topics:

(1) The current state of science outreach and policy.

Surveys and relative social studies were reviewed. Statistical information collected from various sources, including General Social Survey, Wellcome Trust, American Association for the Advancement of Science, and National Science Board, indicate the existence of a significant communication gap between the science community and the general public.

(2) Information regarding major fundamental research concepts.

Reading materials on general research concepts were retrieved from the websites of National Institute of Health, Nature, and several science blogs, such as, Science Policy and Johns Hopkins Health Review. Both the content and the language used in these articles were analyzed and served as examples in developing an appropriate and effective word story for this project.

(3) Particular examples of fundamental research including studies of cell cytokinesis and cellular mechanosensing.

Publications from the Robinson Lab were reviewed. The workflow of their research into cell shape control and mechanosensing were generalized into a series of four strategies. These research strategies serve as a storyline to walk the viewers through a research process for developing novel therapeutics, explaining why and how researchers do what they do.

Wireframe and Word Story Development

As information was collected during literature review, wireframe and word story for the website were developed. The wireframes were helpful in discussing both the content to be included in the program, and the flow of the design. During the initial stage, the wireframe

underwent a series of iterations (**Fig. 11**). The first few versions were hand-written flowcharts used during brainstorming sessions to efficiently exchange ideas. More detailed frames were then combined with text to more completely outline the story. User experience design was also incorporated into the later versions. After several rounds of discussion, three levels of information were identified for the final flowchart (**Fig 12**). The program begins with the question "How does fundamental research help you?" to build a connection with the audience and to

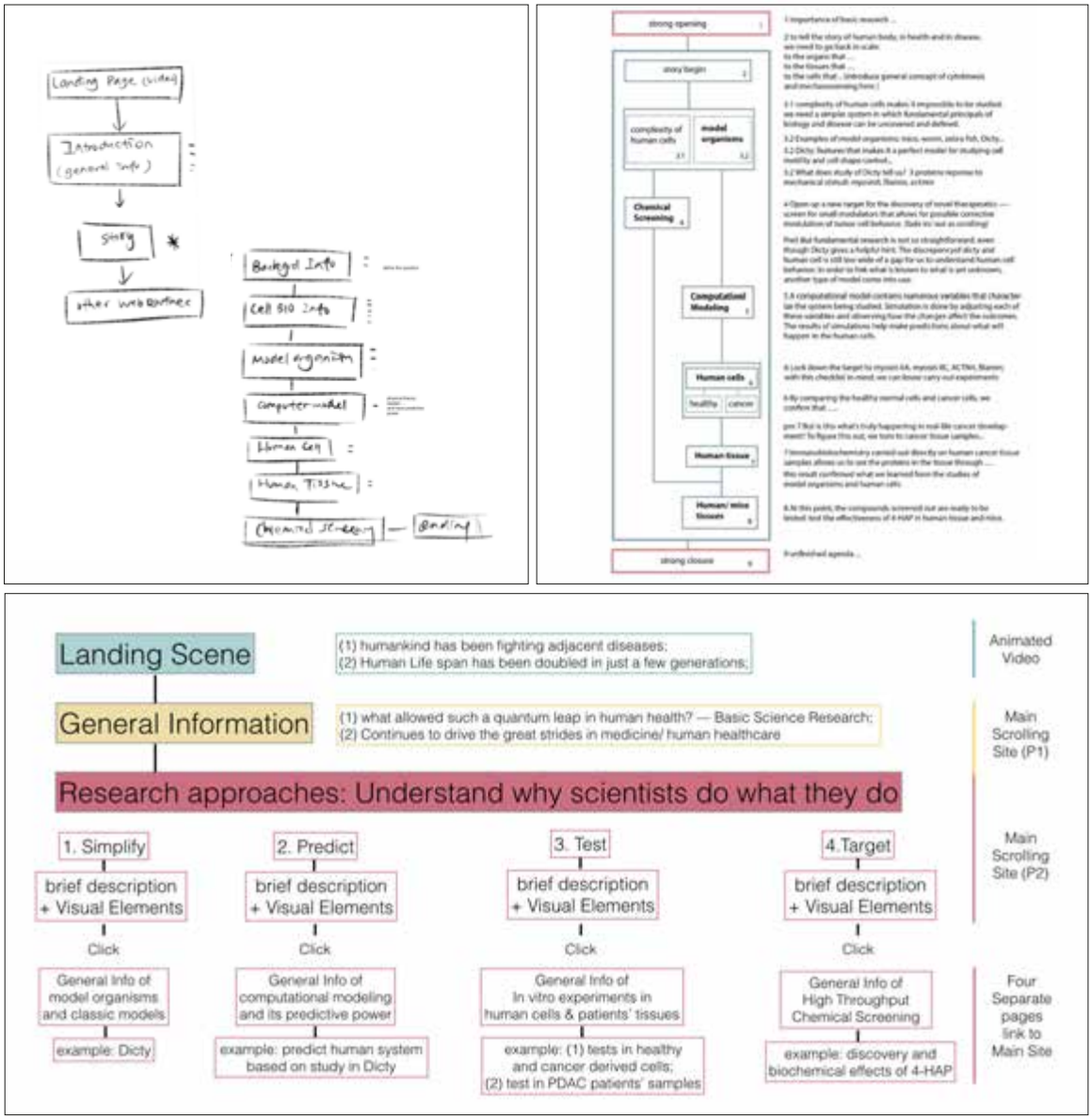


Figure 11. Flowcharts development. Not all text is intended to be read.

inspire thoughts. The second part of the project introduces several aspects of fundamental research ranging from basic information, such as how to more advanced concepts. Once the connection with the viewers is built, the definition and general process of doing research is introduced, followed by the complexity of studying the basic mechanisms of the human system, and corresponding strategies. The third section further explains the strategies. It is designed to increase in detail as the user progressed through the section, covering the general purpose of each strategy, the research approaches used to achieve each goal, and examples of specific studies from Robinson Lab that apply these approaches to investigate molecular and cellular processes of disease.

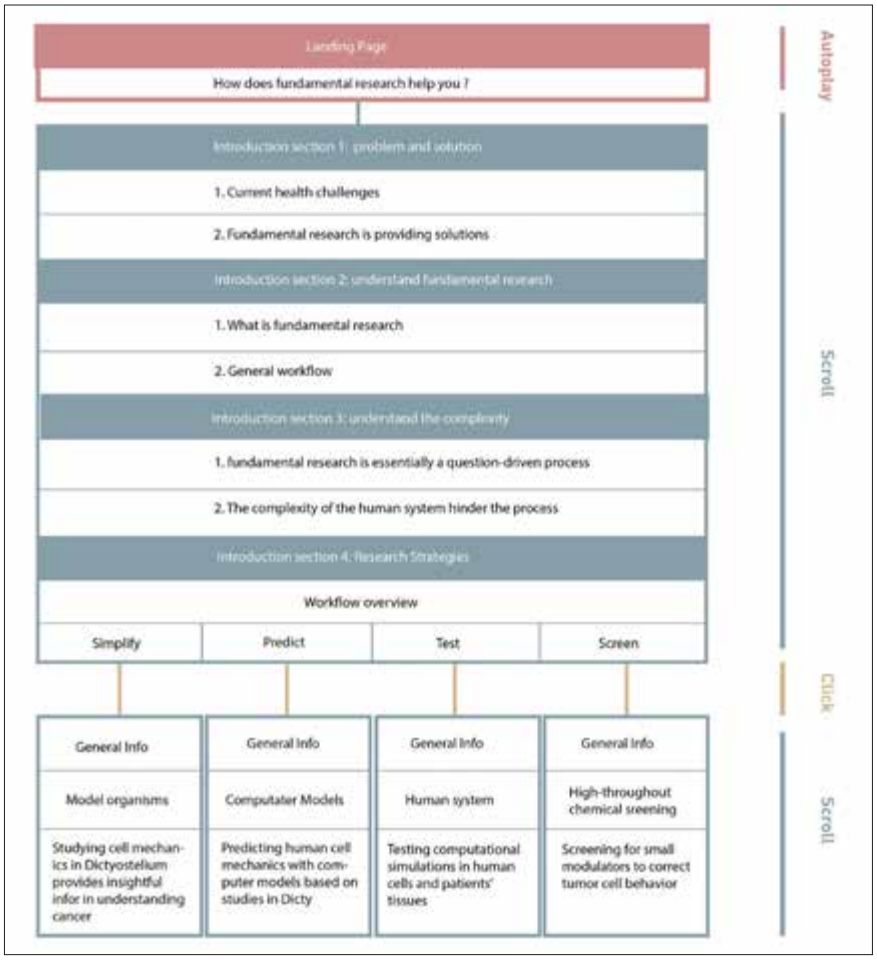


Figure 12. Finalized flowchart. Legible text in subsequent figures.

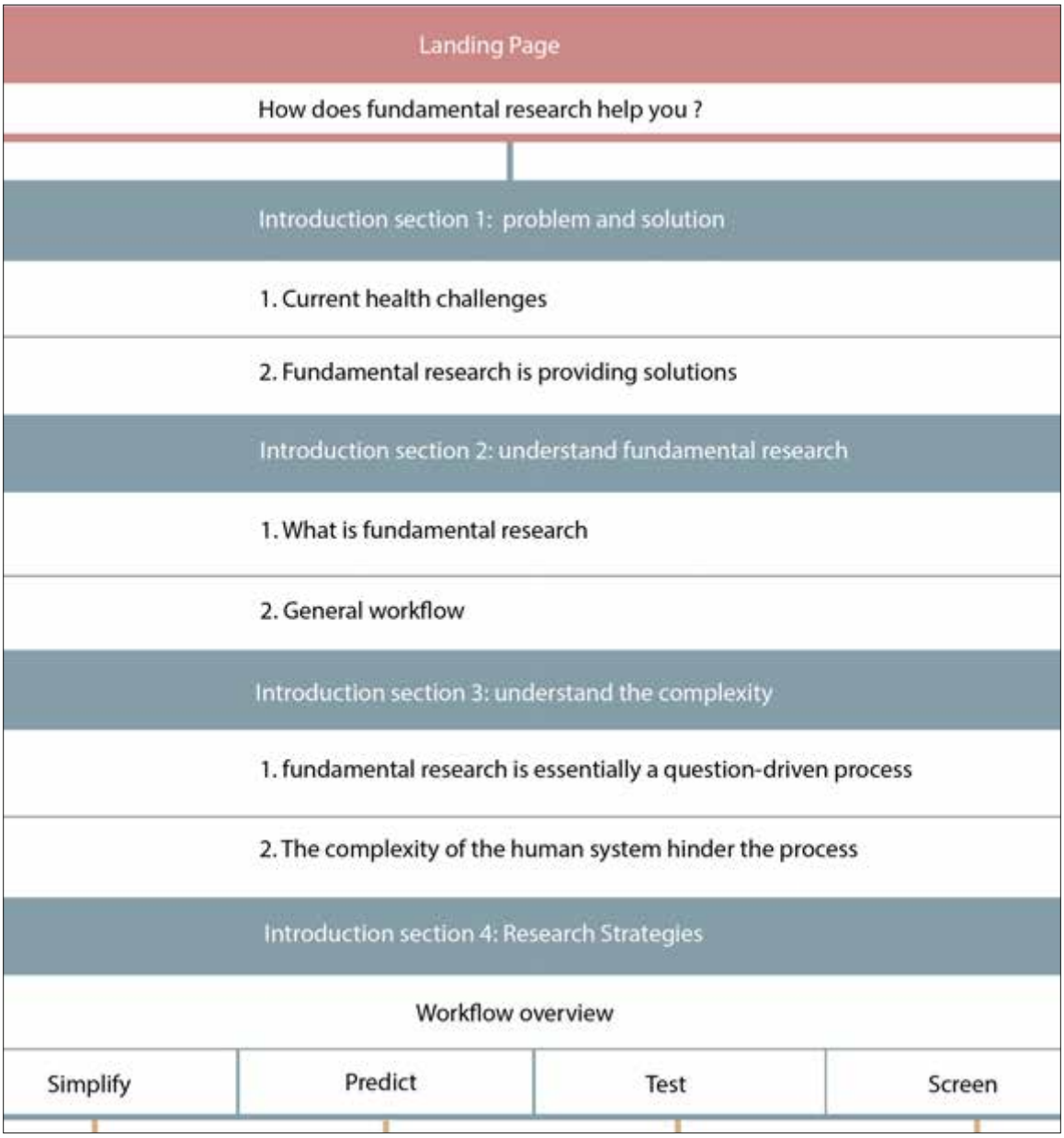
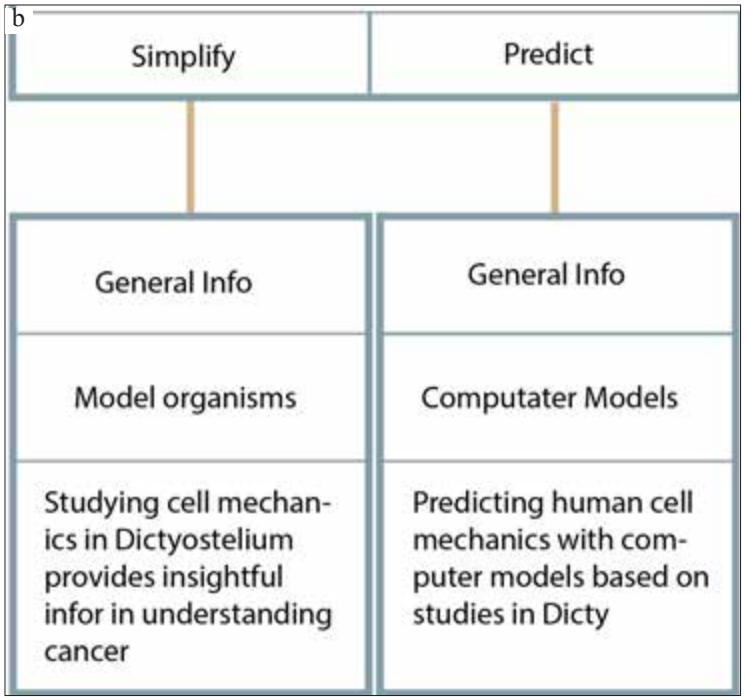
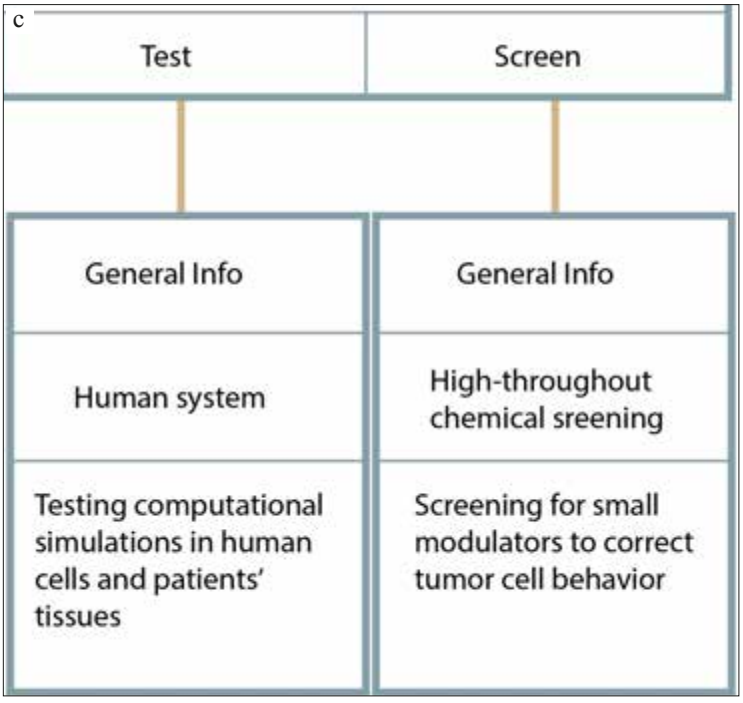


Figure 12a. Finalized flowchart part 1. Landing page and introduction sections.





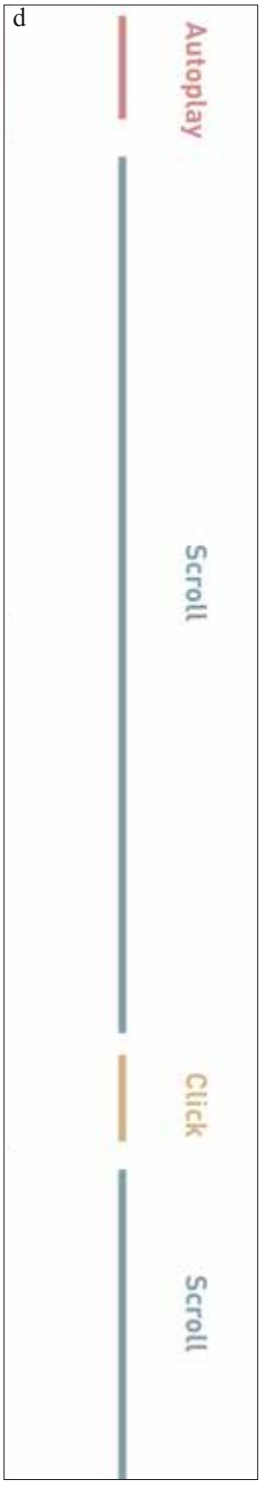


Figure 12b. Finalized flowchart part 2. Child pages Simplify and Predict. **12c. Finalized flowchart part 3.** Child pages Test and Screen. **12d. Finalized flowchart part 4.** User interactivity design.

Storyboarding and Layout Design Process

Storyboards (**Fig. 13**) were created based on the wireframe and word story to show the layout design and intended transitions between various scenes and pages. Storyboards were created using iPad Procreate and were easily exported and modified. The storyboards were shared and discussed with thesis advisor David. Rini, preceptor Douglas Robinson, and other members of his lab to collect feedback on the accuracy and flow of the information. A final version of the storyboards was developed based on feedback and numerous reviews. (Appendix C.)

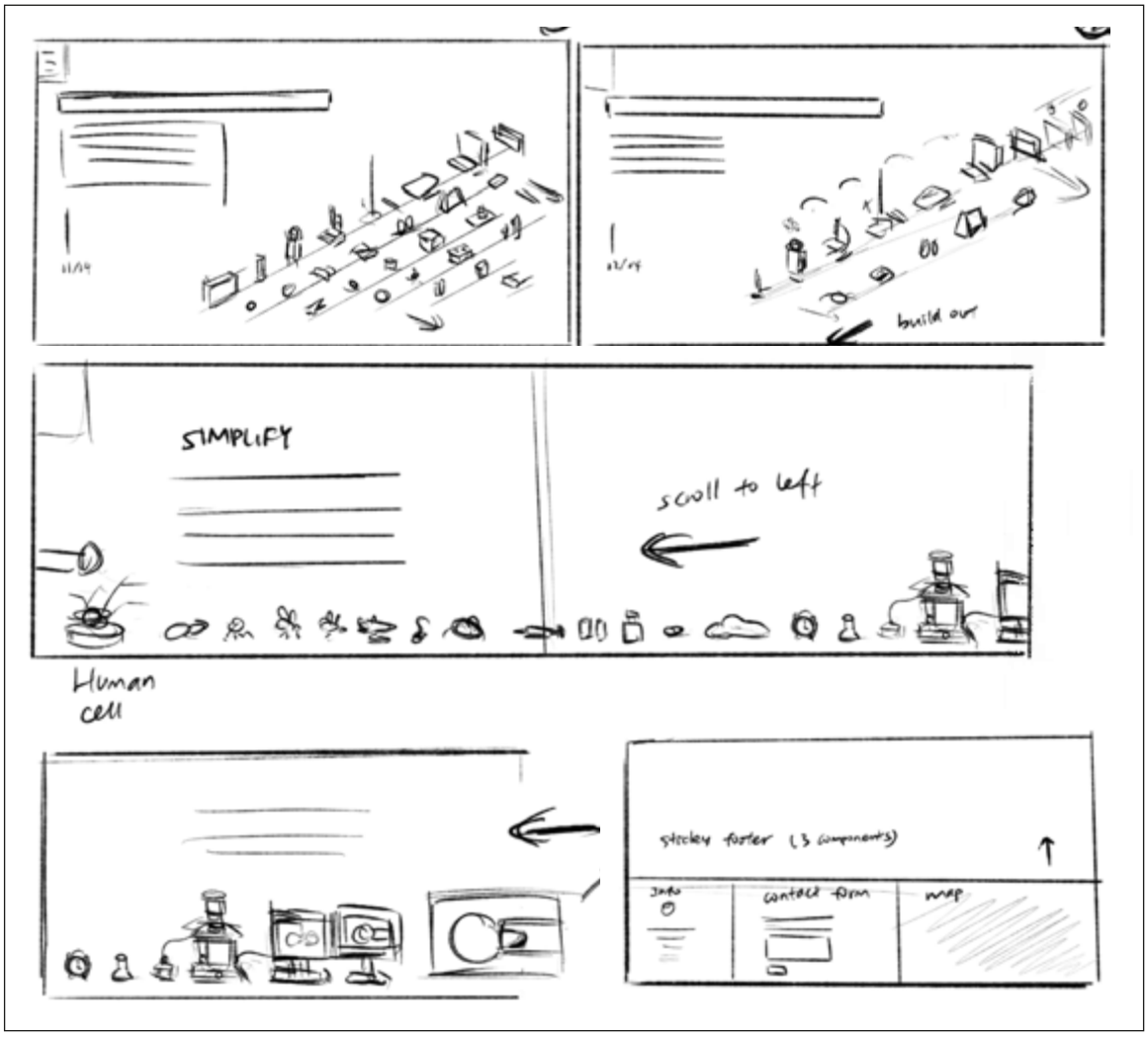


Figure 13. Storyboards development. Text not inteded to be read.

Production Workflow

(1) 3D assets: Draft models and animations were created and key framed based on the storyboards and rendered with basic lighting and materials.

(2) 2D motion elements were created in Adobe After Effects.

(3) User interface designs were produced in Adobe Illustrator.

(4) Animatics (draft prototype) were created in Adobe After Effects.

(5) Feedback was collected throughout the process.

(6) Final renders of 3D assets were set up with well designed lighting and materials.

(7) Animated video was created in Adobe After Effects.

(8) Development of scrolling video site with Scrolling triggered Video Playback technique in JavaScript, and HTML Canvas.

(9) Long-term feedback will be collected through the Contact Form on the website.

List of Softwares
Maxon Cinema 4D
Adobe After Effects CC
Adobe Illustrator CC
FormatFactory
Keynote
Procreate

Figure 14. List of software used.

3D modeling with Maxon Cinema 4D

The majority of the visual elements are 3D models created in Maxon Cinema 4D. A style was developed to match the overall program design with particular consideration given to modeling and render requirements.

(1) Low-polygon modeling

The models were created in a Low-Poly style utilizing the Polygon Reduction deformer (**Fig. 15**). Phong tags were removed or the "Phong angle" was turned down to "20 degree".

(2) Isometric projection with camera setting

Isometric projection shows the depth of 3D objects without foreshortening or distortion. Isometric projection was applied to the models by setting the projection of the 3D camera to "isometric" (**Fig. 16**). Note that the camera can not be rotated once isometric projection is on.

Figure 15. Polygon reduction. Deformer settings.

Figure 16. Isometric projection. Camera set up.

3D simulations with Maxon Cinema 4D

All 3D animations were completed in C4D, using simulations, dynamics, MoGraph and deformers. In addition, some animations required limited keyframes.

(1) **Cellular simulation with displacer**

The simulation (**Fig. 17**) is composed of a sphere and multiple displacers, organized under a single null object. Turning one or a combination of displacers on and off produced different textures on the cell surface, resulting in effective simulations of cellular deformation to represent healthy and infected cells. Subdivision Surface was applied to the folder to smooth the cell surface during the animation.

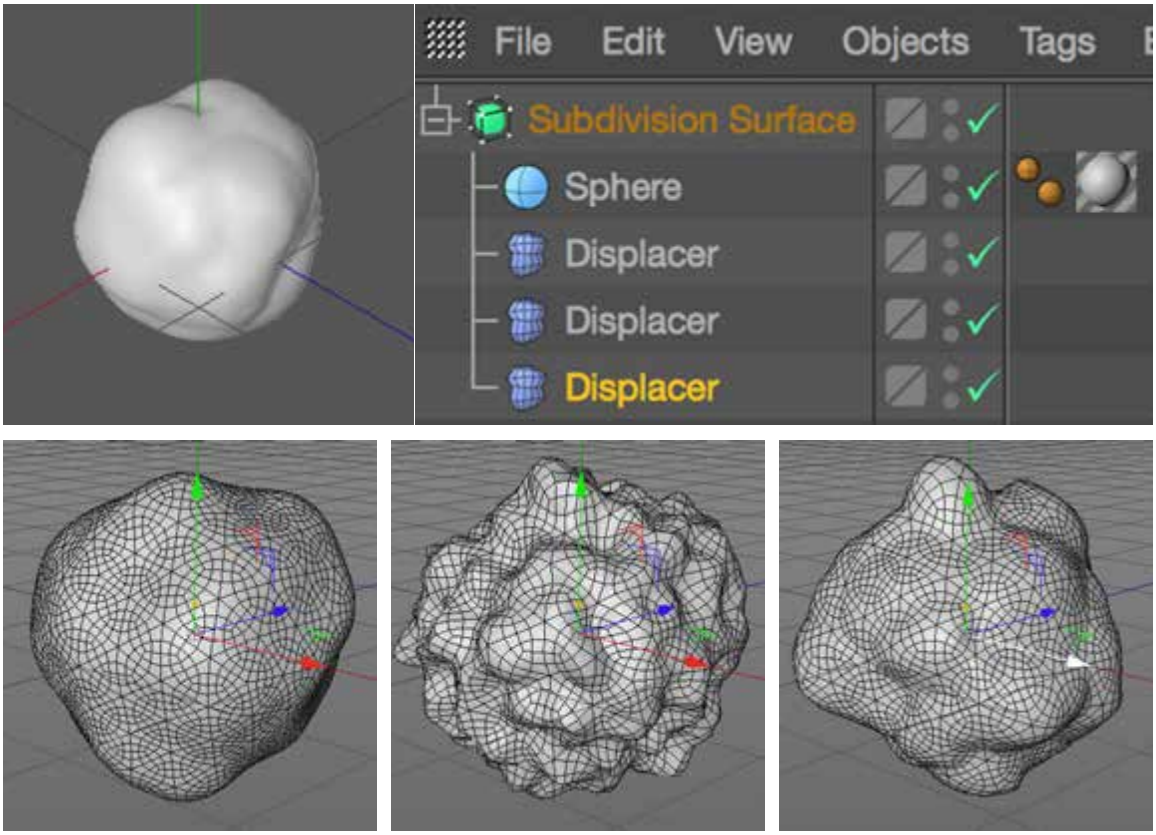


Figure 17. Cellular simulation settings. A combination of multiple displacers .

Displacer (**Fig. 18**) is a deformer in Cinema 4D that applies noise patterns to the surface of an object to produce an organic look. The noise pattern "Voronoi 1" was selected in this case. Color 1 (originally black) and 2 (originally white) were reversed to further highlight the valleys and ridges of the pattern mapped onto the cell surface. Animation speed was set at 0.5 - 2.5 to allow the cell to change shape without keyframes. A global scale of "600-1000%" was set to make the noise pattern look more subtle. Displacer height, which determines the overall strength of the deformer was set to "10-20 cm". The final result was an organic, bumpy appearing cell.

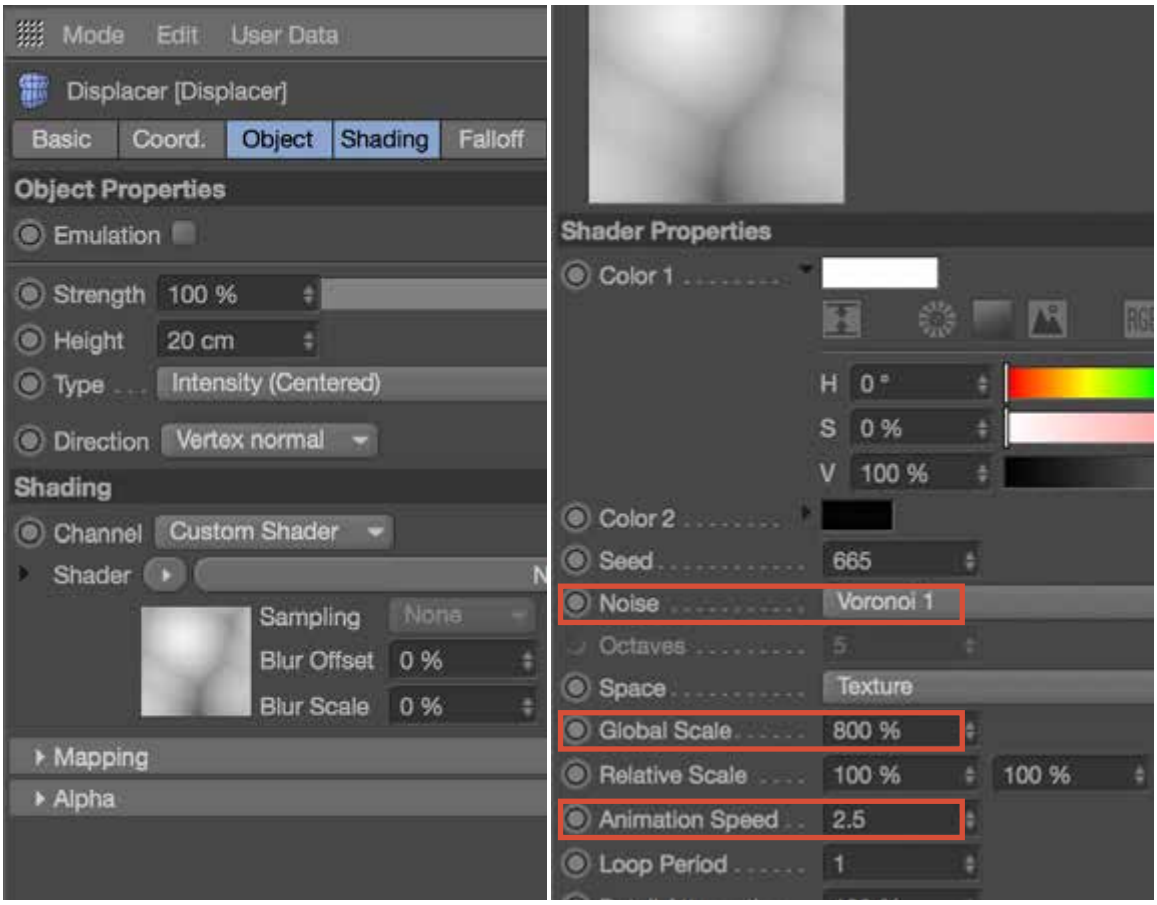


Figure 18. Example of Displacer settings. Height, noise pattern, global scale and animation speed were explored and tested.

(2) Cell tearing simulation with Cloth Simulation tags

The simulation (**Fig. 19**) is composed of a cell (textured with displacers as previously mentioned), with two smaller spheres inside, serving as the forces that tear the cell apart. "Cloth Surface" was applied to the cell, providing thickness. The spheres were set as "Icosahedron" and "Render Perfect" was unchecked. "Subdivision Surface" was then applied to smoothen the polygons during tearing.

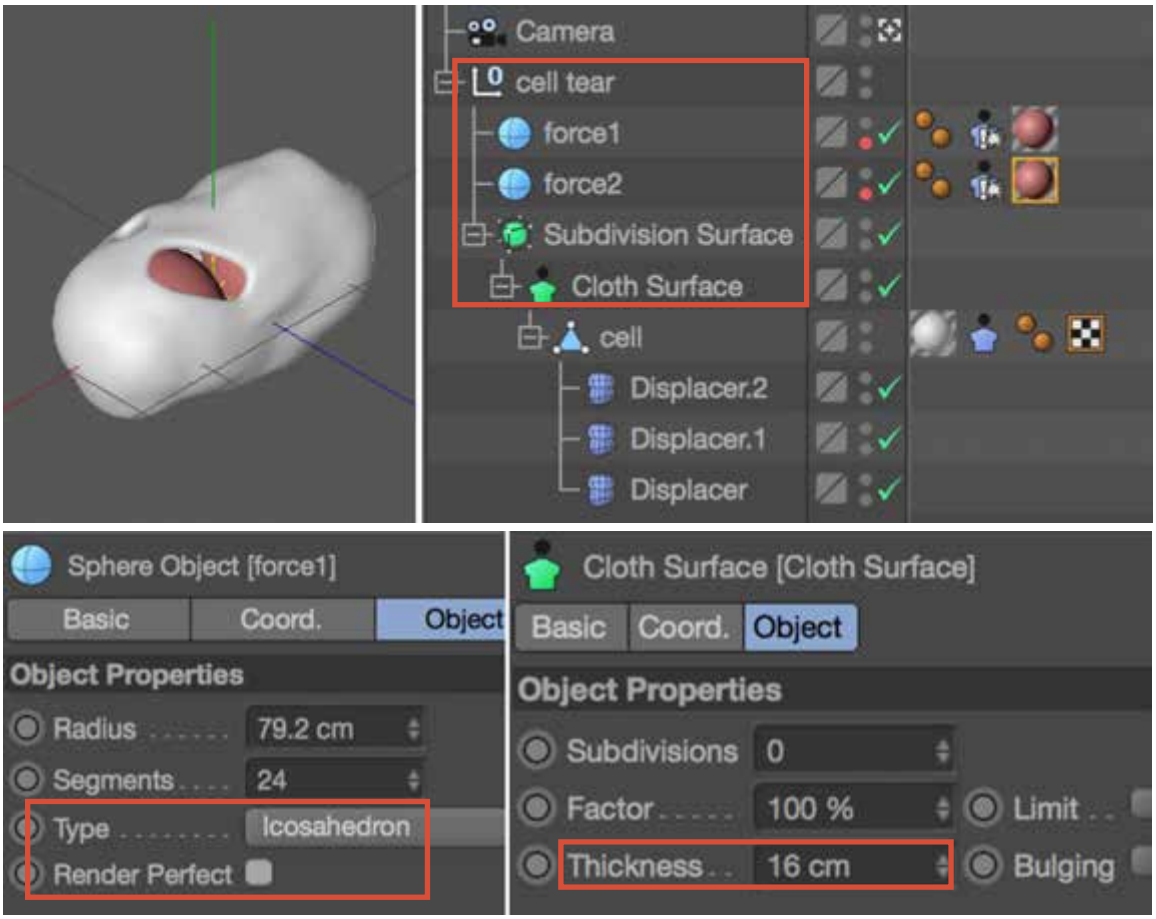


Figure 19. Cell tearing simulation. Cloth Surface, Subdivision Surface and force generation.

The positions of the spheres were keyframed to move outwards and generate the force that tears the cell apart (**Fig. 20**).

Figure 20. Generating force. Keyframe the positions of the spheres along the timeline.

Simulation tags (**Fig. 21**) were then applied to the objects. Cloth Tag (tag > simulation tags > cloth tag) was applied to the cell. "Use Tear" was checked and "Tear" was set to 160%. Gravity was set to "zero" so the cell did not fall. The "cell" was made "Editable" to ensure the smoothness of the tearing simulation. Cloth Collider Tag (tag > simulation tags > cloth collider tag) was applied to the small spheres with the default settings.

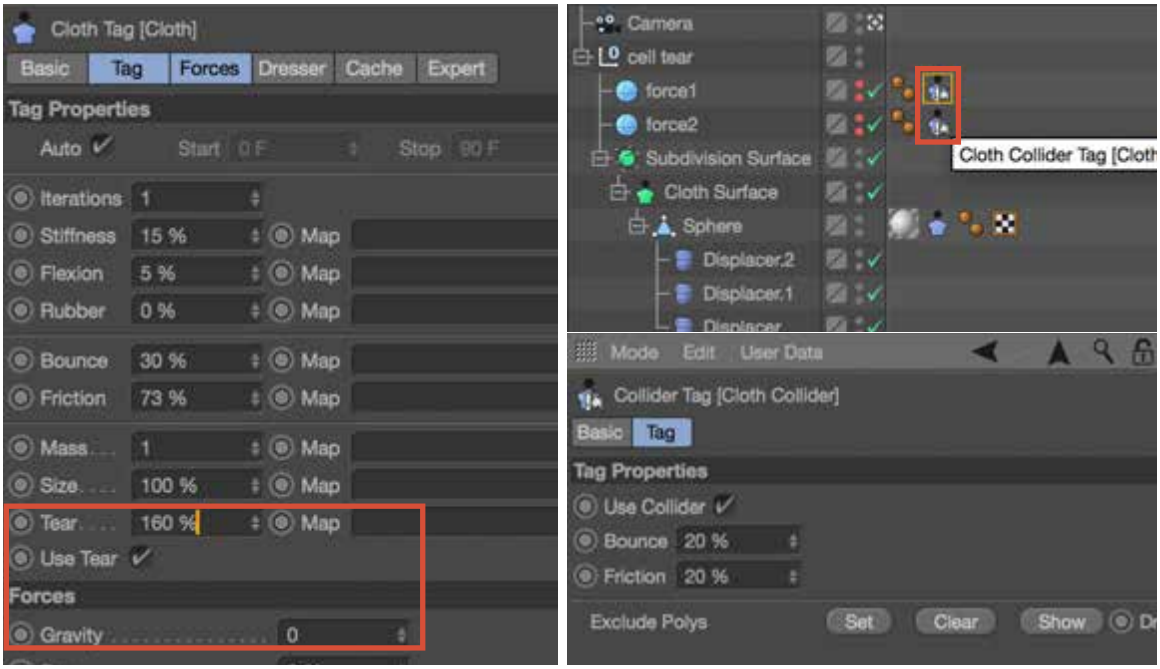


Figure 21. Simulation Tags settings. Cloth Tag and Cloth Collider Tag.

(3) Cell deformation and movement using soft body dynamics

This simulation (**Fig. 22**) is composed of 13 spheres (cells), in a cube acting as a bounding box. Turbulence was added to the scene, providing the external force for cells to move randomly. The spheres were positioned as close to each other as possible. Note that the spheres should not touch each other at frame zero, otherwise C4D might crash.

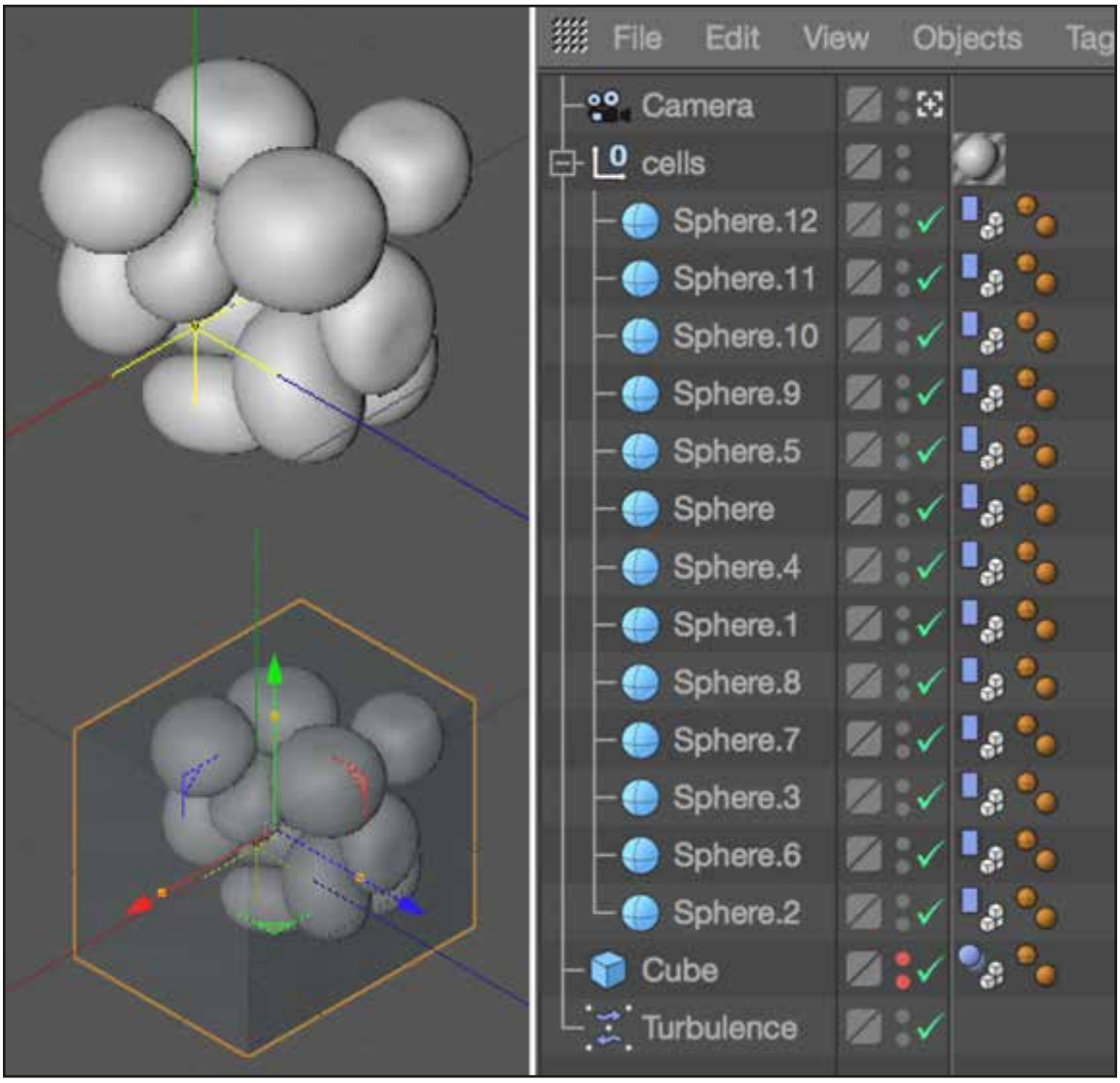


Figure 22. Cell deformation simulation. Multiple spheres inside a cube.

Soft Body Tags (**Fig. 23**) were added to all the spheres. Parameters including structural spring, stiffness and pressure were adjusted to achieve the desired cell deformability. "Pressure" makes the cells expand like balloons to fully occupy the volume of the bounding box once hitting the play button. This causes the cells to squeeze together and interact with each other.

Figure 23. Soft Body Dynamics. Structural, Stiffness, Pressure.

Collider Body Tag (**Fig. 24**) was added to the cube. "Static Mesh" was selected under Shape.

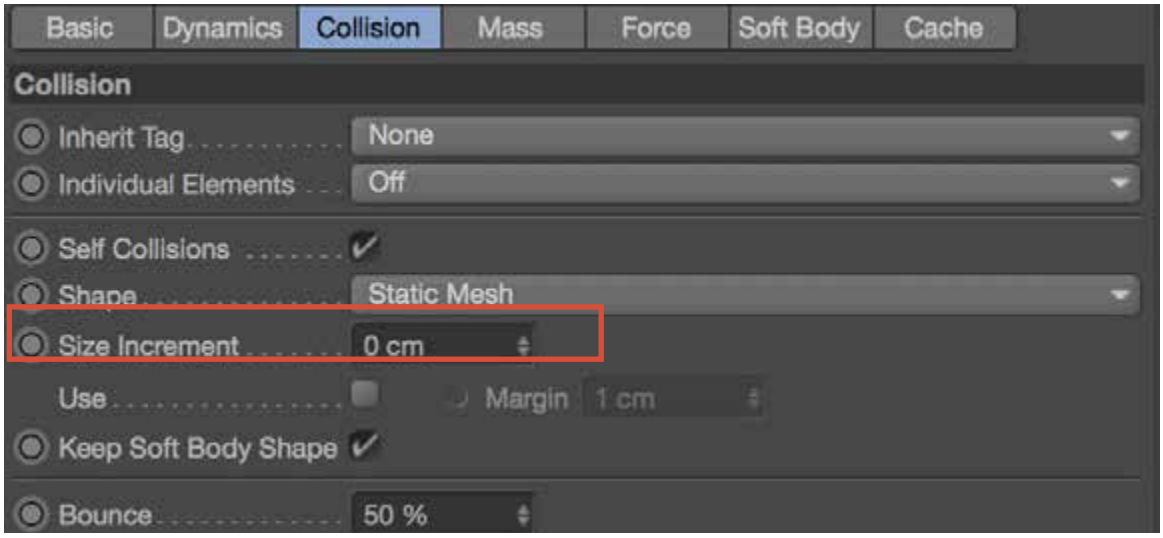


Figure 24. Collider Body Simulation. Static Mesh.

Gravity of the 3D world was adjusted under Project dynamics (Cmd + D). from the default of 1000cm to 10cm to prevent the objects from falling. Turbulence (Simulate > Particles > Turbulence) was applied to the scene. Scale and Frequency were set to 100% in this case.

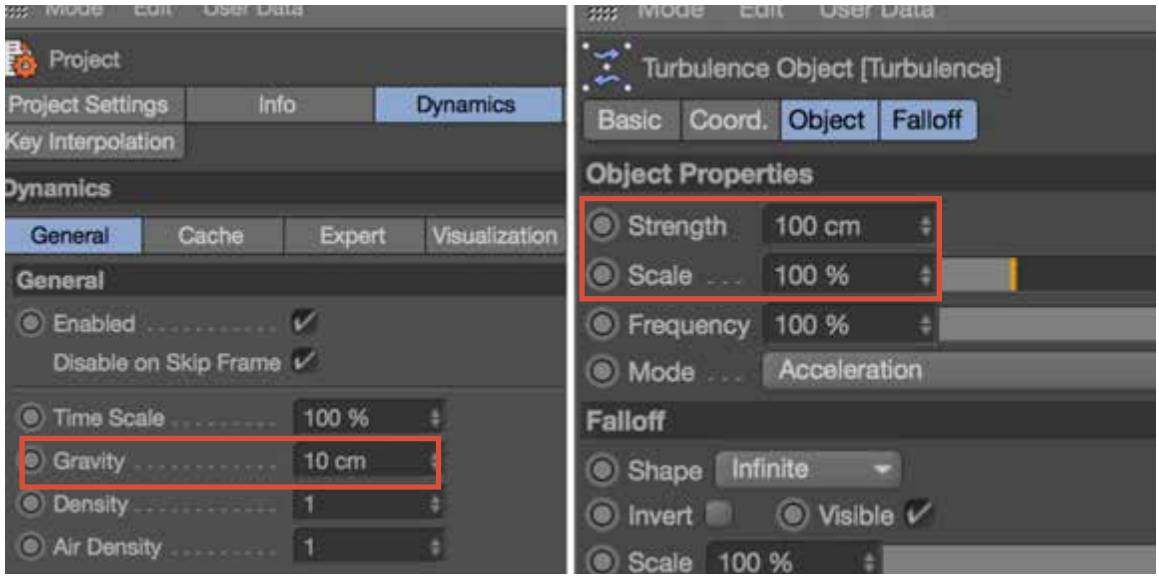


Figure 25. Gravity and Turbulence. Reduce Project Gravity, increase Turbulence Strength and Scale.

(4) DNA helix winding with twisting

The simulation (**Fig. 26**) is composed of straight splines that represent the backbone and base pairs of the DNA helix. Each spline is a child of a Metaball. The Hull Value and Subdivision level are shown below. One of the base pairs was separated from the main spline to receive materials with different colors, representing gene mutation. Twist deformer was applied to each spine. The angles (0 - 720 degree) were keyframed to animate the winding and unwinding process of the DNA double helix.

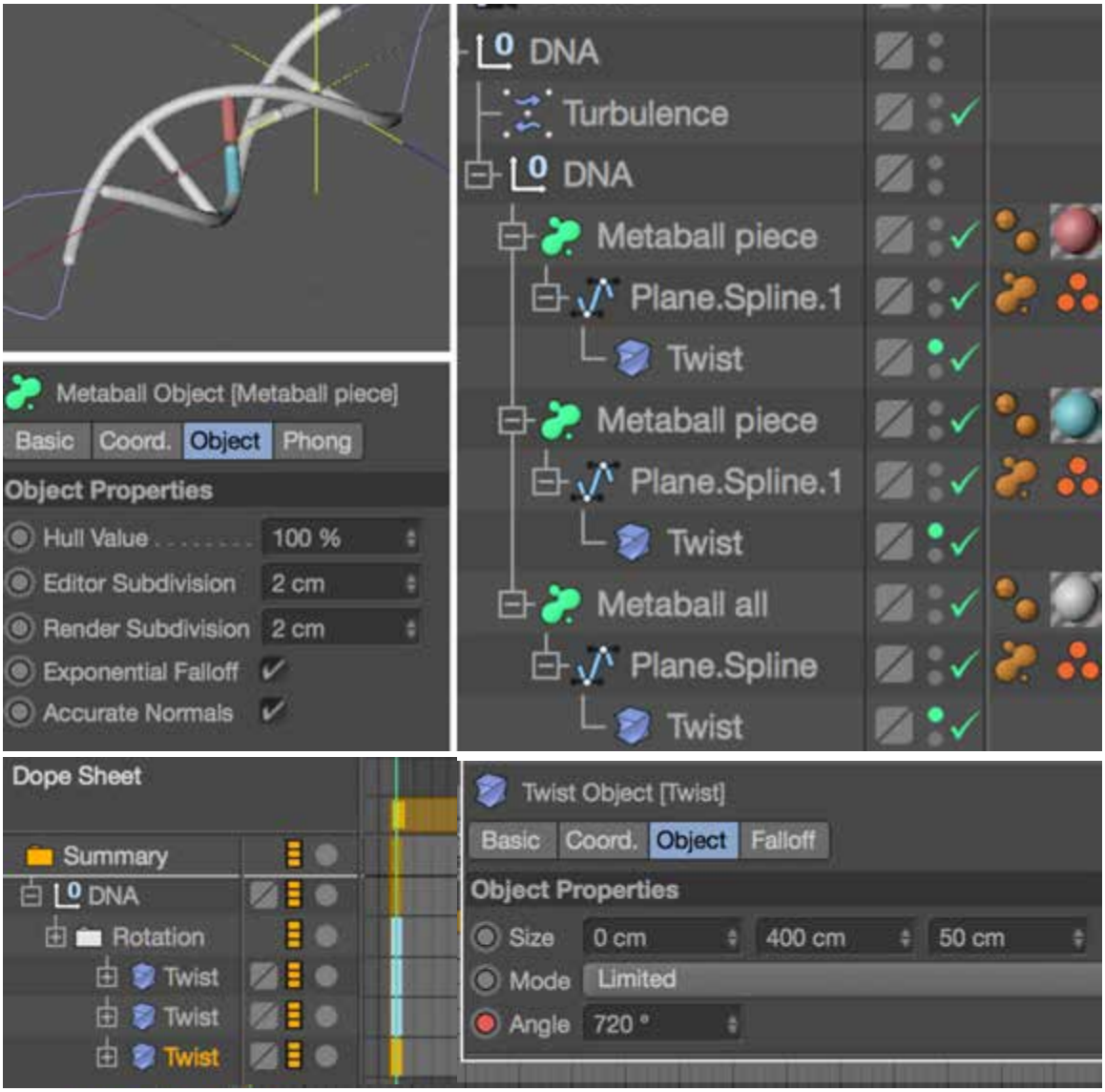


Figure 26. DNA helix simulation. MetaBall and Twist Angle.

(5) Slime Mold movement with Metaball, Metaball tag and MoGraph

This simulation (**Fig. 27**) is composed of a static plate, and a dynamic "slime mold", consisting of a clone of spheres, and a cylinder to represent "agar", which are children of the same Metaball so that the "agar" will move along with the Cloner when acted on by the Formula effector.

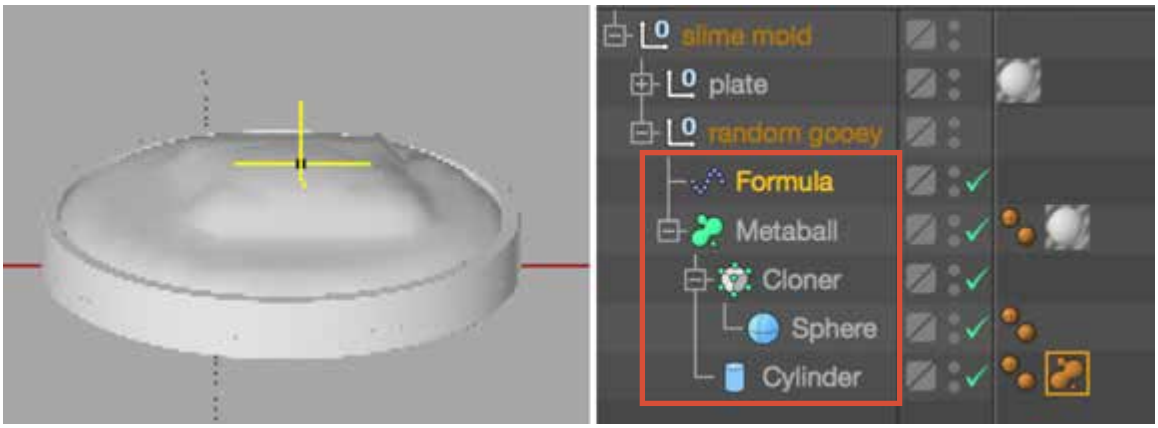


Figure 27. Slime Mold Movement. Cloner, Metaball, Formula.

Metaball is effective on spheres and splines, but often does not work consistently with shapes like cylinder or cubes. Hence, a Metaball tag (Tags > Cinema 4D Tags > Metaball Tag) was added to the cylinder to achieve a better result. Strength and Radius were set to 55% and 15cm, respectively.

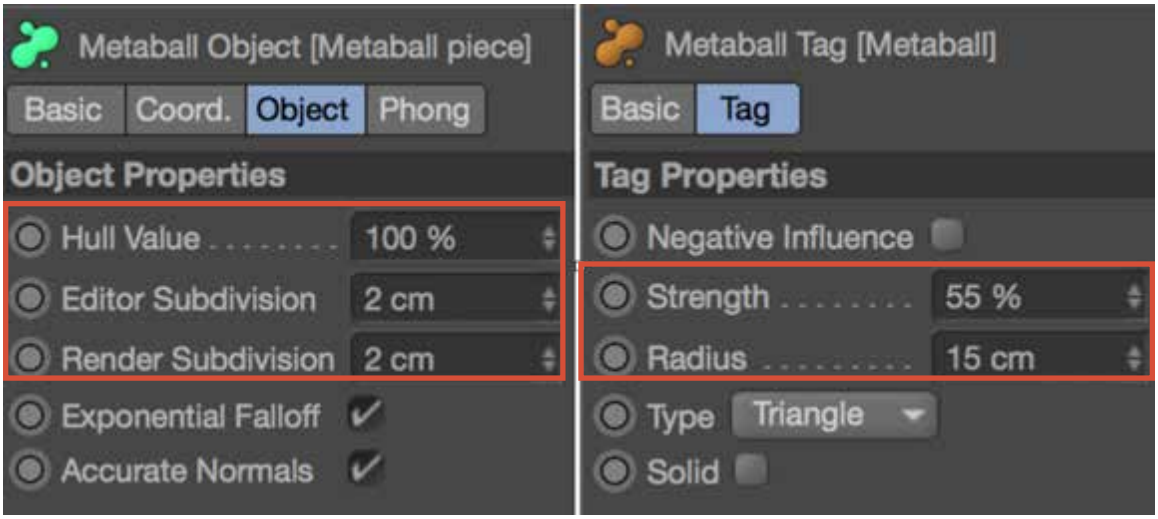


Figure 28. Metaball and Metaball Tag. Hull value, Subdivision, Strength, Radius were adjusted.

MoGraph is a toolset in C4D that creates various motions effects. The basic shape of the "slime mold", was created using the Cloner (MoGraph > Cloner > Grid Array) (**Fig. 29**), which was animated with MoGraph effectors. A Formula (**Fig. 30**) effector was used in this case, and a Sin wave was applied.

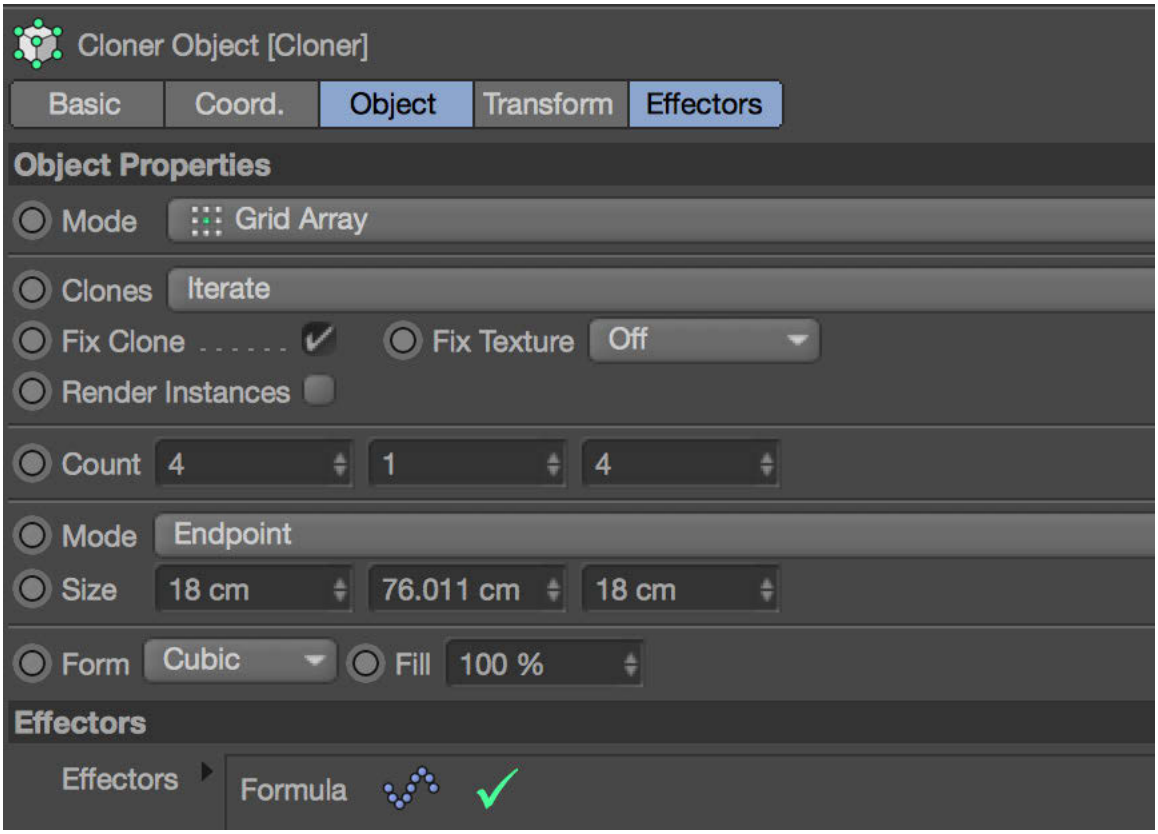


Figure 29. Cloner settings. Grid Array.

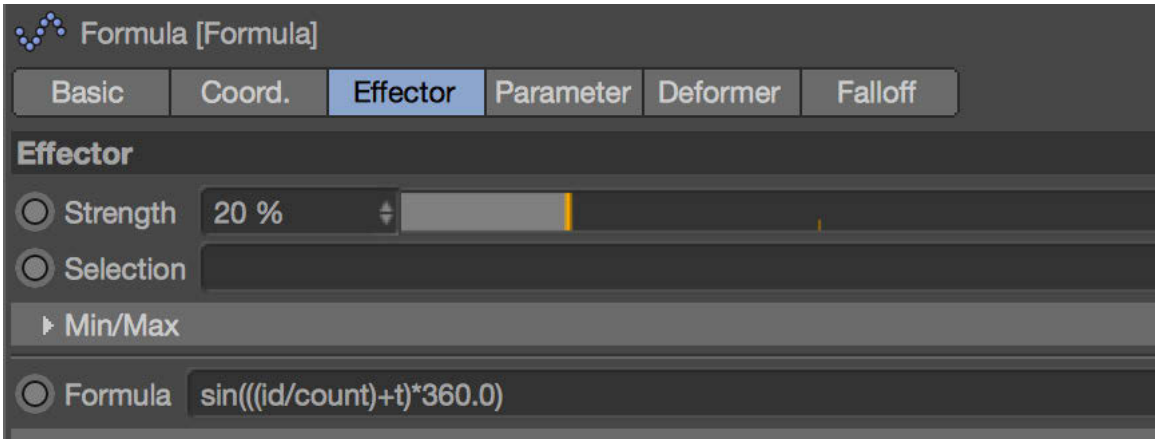


Figure 30. Formula Effector settings. Sin wave.

Lighting and Materials

Lighting

To achieve a clean style without dramatic shadows, **Illuminati** (**Fig 31**), a free plugin, was used to light up the entire scene. **Light intensity** was set to between 50 - 60% to prevent overexposure. Inner and outer **angles** were adjusted to show details in the shadows.

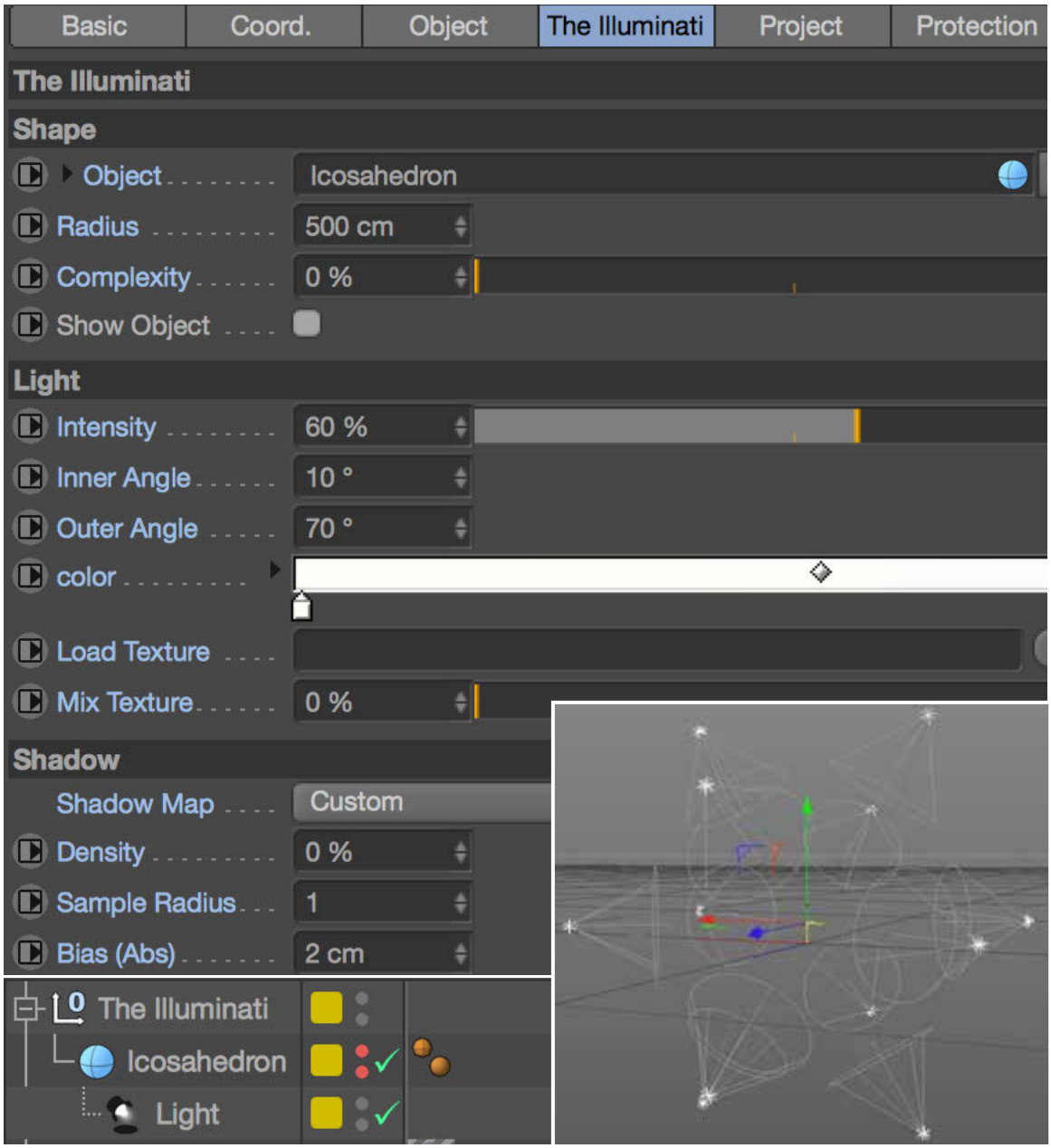


Figure 31. Illuminati settings. Noted that Illuminati renders much faster than Global Illumination.

Materials

Materials for most objects were kept simple with only Color and Reflectance channels turned on. The color was set to 80-100% white. Specular strength and width were adjusted to provide a slight shininess. Settings are shown below (**Fig. 32**).

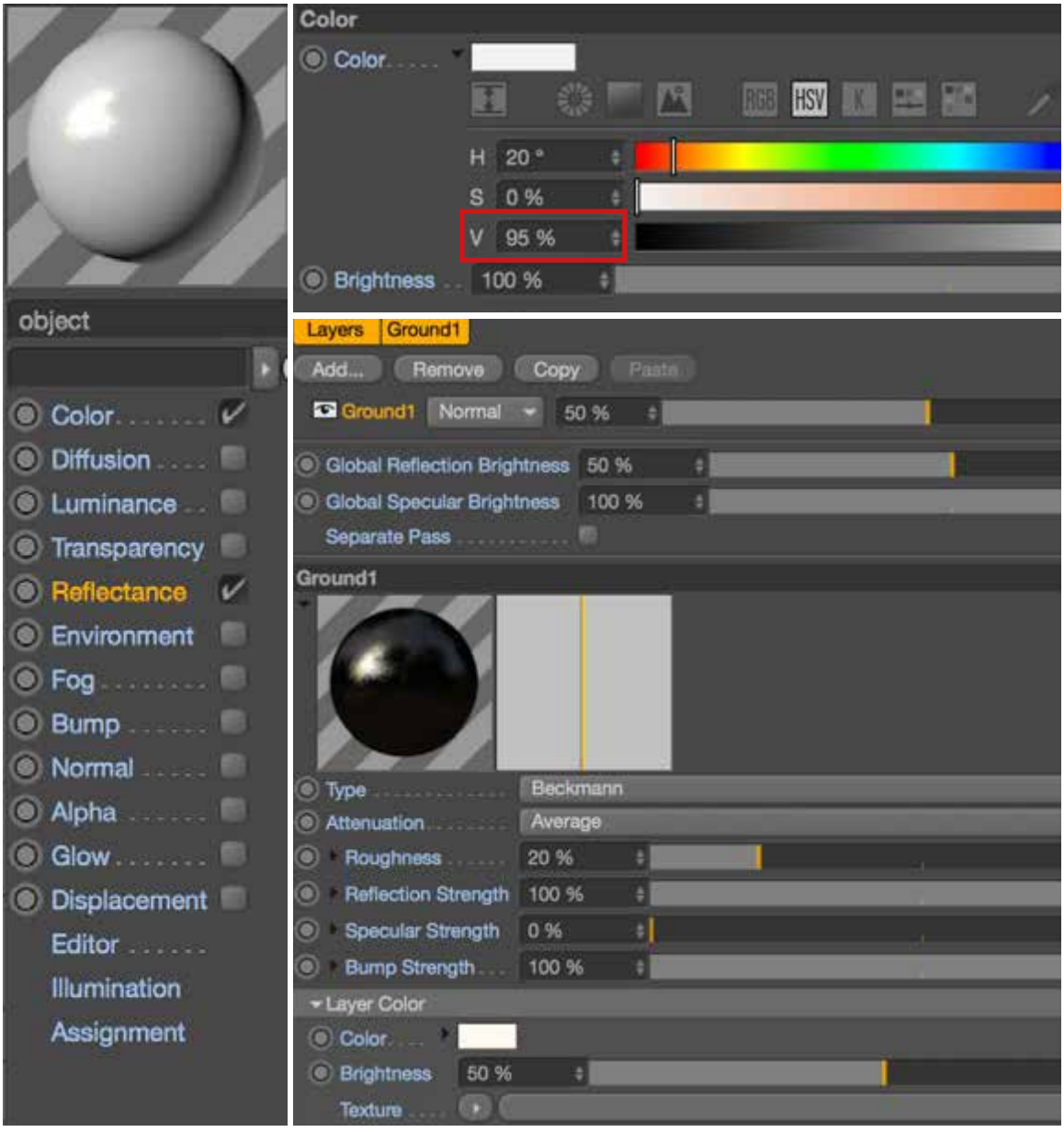


Figure 32. Material settings. Only Color and Reflectance channels were turned on. Noted that "V" of the Color channel was adjusted from 85% - 100% for different objects to avoid overexposure on some objects that have more polygons directly facing the light.

Render Settings

The Physical Renderer (**Fig. 33**) was used to render all the 3D objects, animations and scenes. The sampling quality was set to Medium, which improved the the final appearance compared to Low, and rendered much faster than the High setting. Output was set to 1280 (Width) x 720 (Height) pixels with the resolution of 180 DPI. Ambient Occlusion (AO) was added, cached, and rendered on a separate layer. The maximum ray length was increased from the default of 100cm to 150 - 200cm to intensify the soft shadows that occur in the crevices of the objects and the planes where the objects touch the floor. The color was changed from black to dark blue to match the background color.

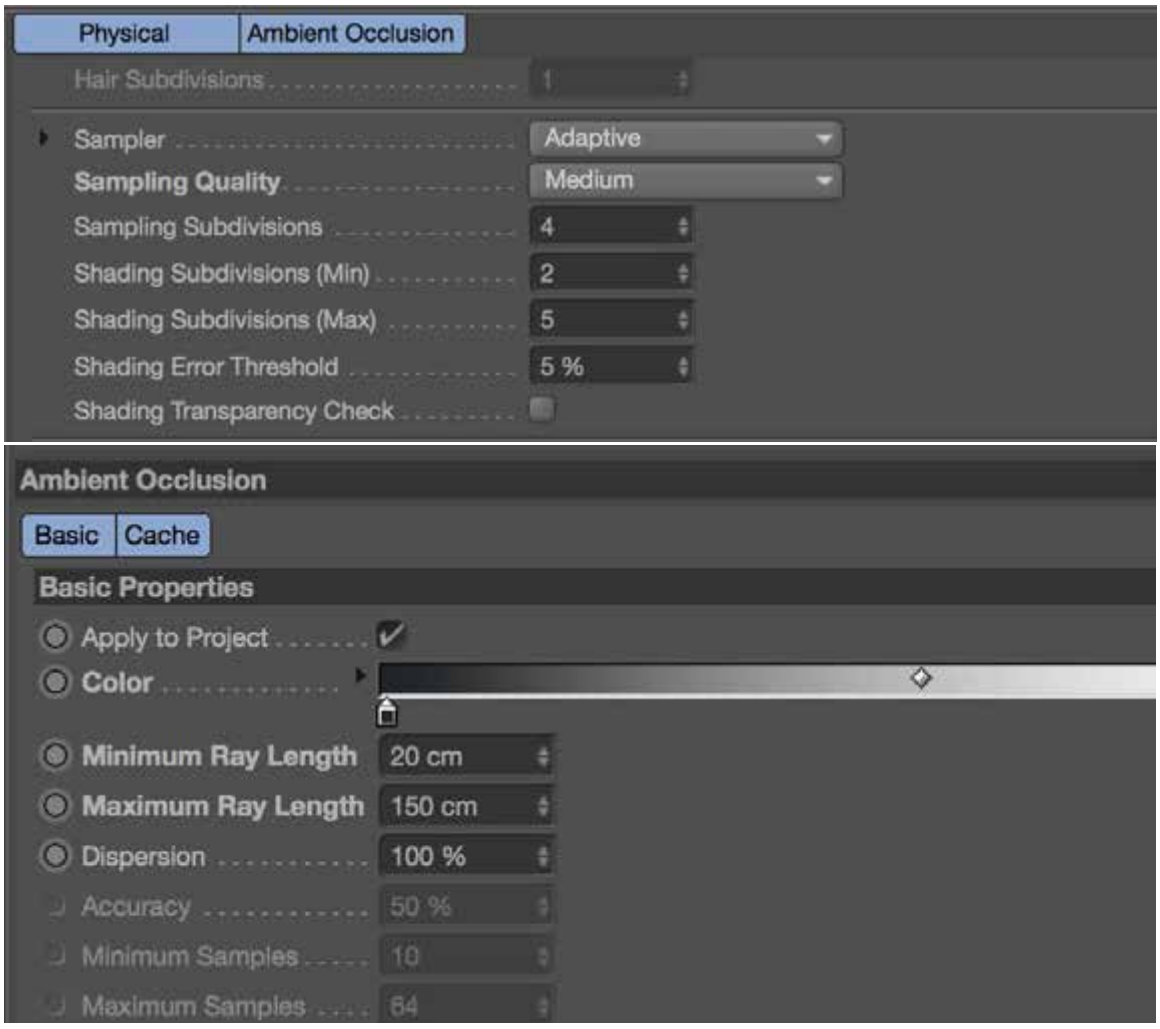


Figure 33. Render settings. Physical Render and Ambient Occlusion.

Render with Take System

Cinema 4D's Take System (**Fig. 34**) was used to render multiple objects separately from the same file. Each "Take" stores any action applied to the objects, including turning the visibility on and off, adding tags and changing camera angles. Note that that relevant Take must to be selected in order to change the settings,. In this way, objects can be automatically rendered one after another by indicating the Takes to be rendered (**Fig. 35**). In addition, Takes can be set as a Child of another Take (**Fig. 36**), to inherits the actions from its Parent.

Figure 34.Take System. Create new Takes and store the visibility of each object accordingly.

Figure 35. Mark the Take. Rendered Marked Takes to Picture Viewer.

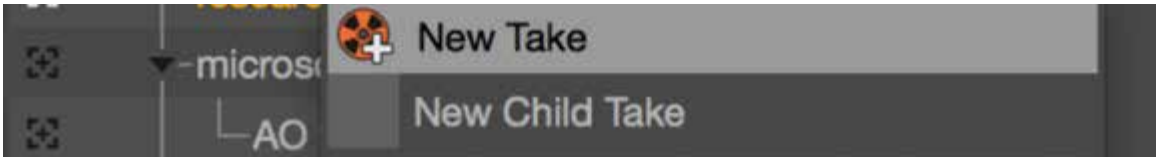


Figure 36.Child Take. Inherit settings from its Parent Take.

Specific render settings can be assigned to each take (**Fig. 37**), whether it is a static or an animated object. Different render variables (Output, Ambient Occlusion, etc) were set up and saved with specific labels under Render Settings. Then a list of these already saved Render settings was displayed in the Take manager, which could be assigned to the Takes, respectively.

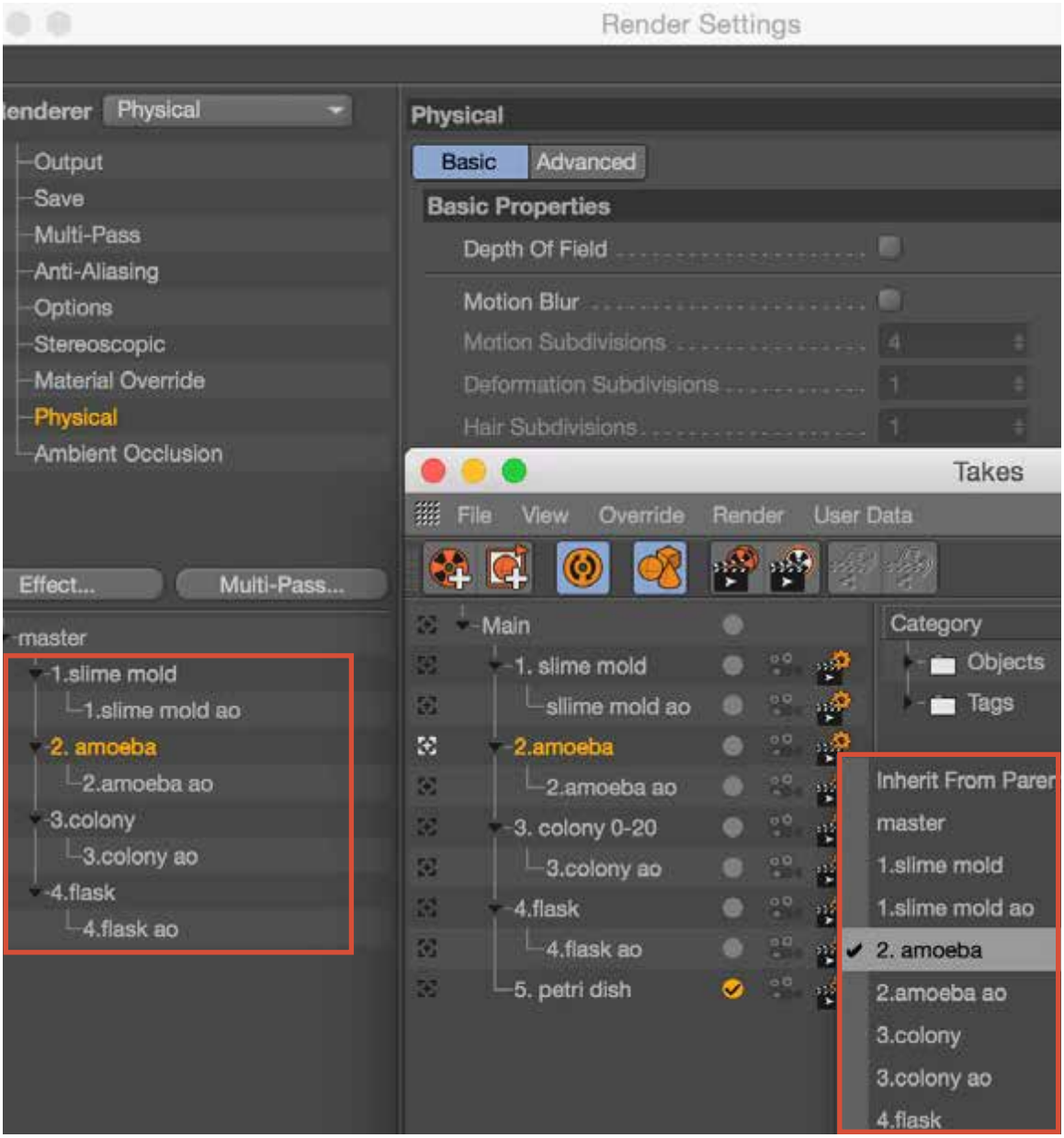


Figure 37. Render settings assigned to Takes.

User Interface Design in Adobe Illustrator

2D and 3D assets and draft renders (if not finalized) were imported into Adobe Illustrator to develop the user interface design (**Fig. 38**). The visual elements and text were composed on multiple Artboards and layers. Artboards allow the presentation of the interface designs for each page all at once to ensure consistency of the style. This method allows the text layout to be directly copied and pasted into Adobe After Effects text layers, keeping the character style consistent, thereby streamlining the workflow.

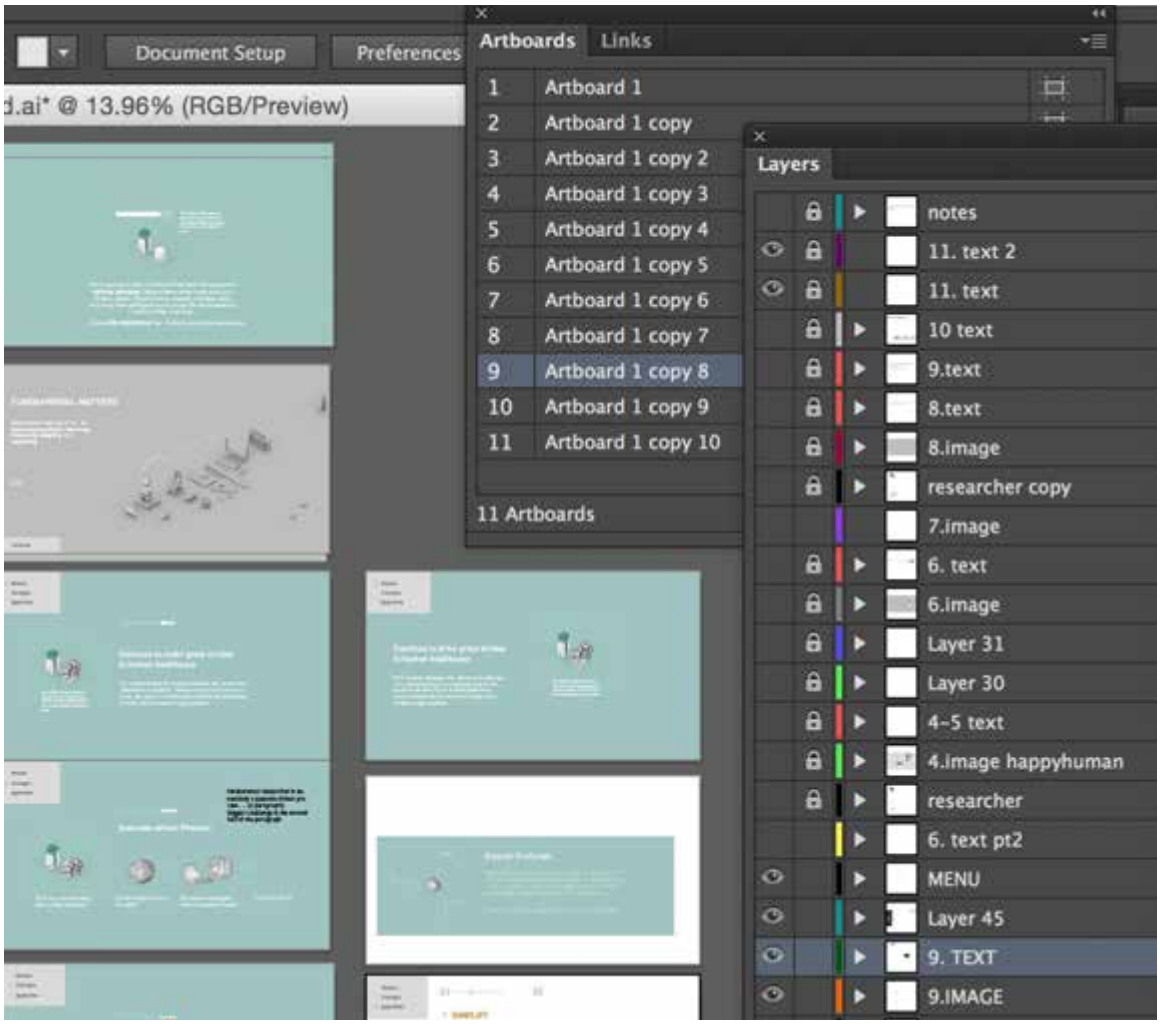


Figure 38. An example of Adobe Illustrator Interface. Multiple artboards and layers created for the user interface design. Text not intended to be read.

2D motions with Adobe After Effects

2D motion elements were added to the design to deliver information and guide the viewers through the interface. All of these elements were created in Adobe After Effects (AE).

Trim Paths (Fig. 39) was used to efficiently animate line motions without using masks. The Animated icon" Scroll to explore" was created this way. Trim-path was added to the layer by > Shape Layer > click the play button next to "Add:" > choose "trim paths". "Start" and "End" were adjusted between 0 - 100 %. Keyframes were set for "Start" and/or "End" to create the desired motion.

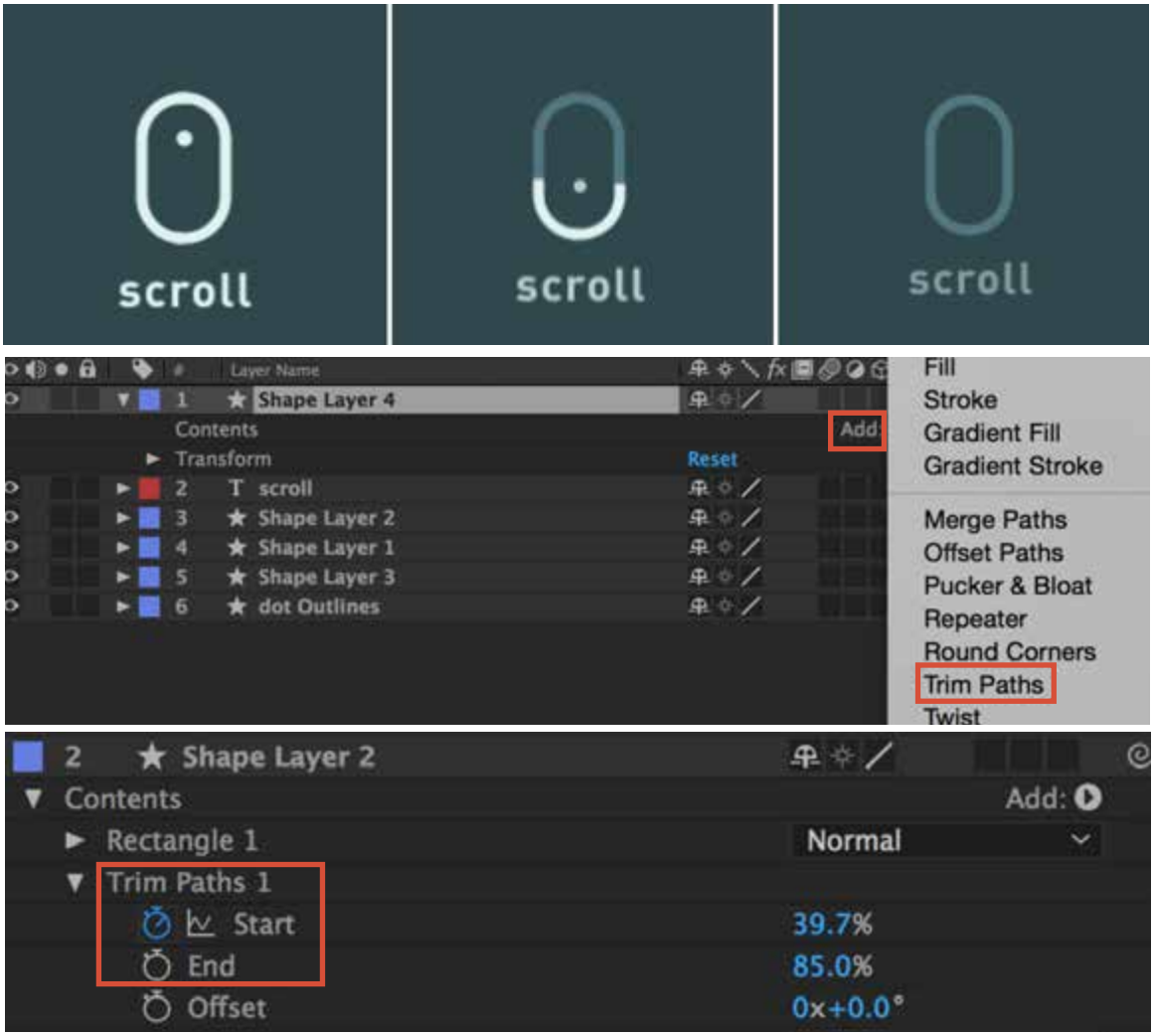


Figure 39. Animated Icon created using Trim Paths. Start and End features were key framed.

Creating Animated Prototype in After Effects and Keynote

Animated prototype was created in After Effects (**Fig. 40**) for pre-visualizing the interactive design, including pacing, the flow of the information, and the overall effectiveness of the motions. Images, texts composed in Adobe Illustrator, as well as PNG sequences (**Fig. 41**) rendered in C4D, were imported into Adobe After Effects.

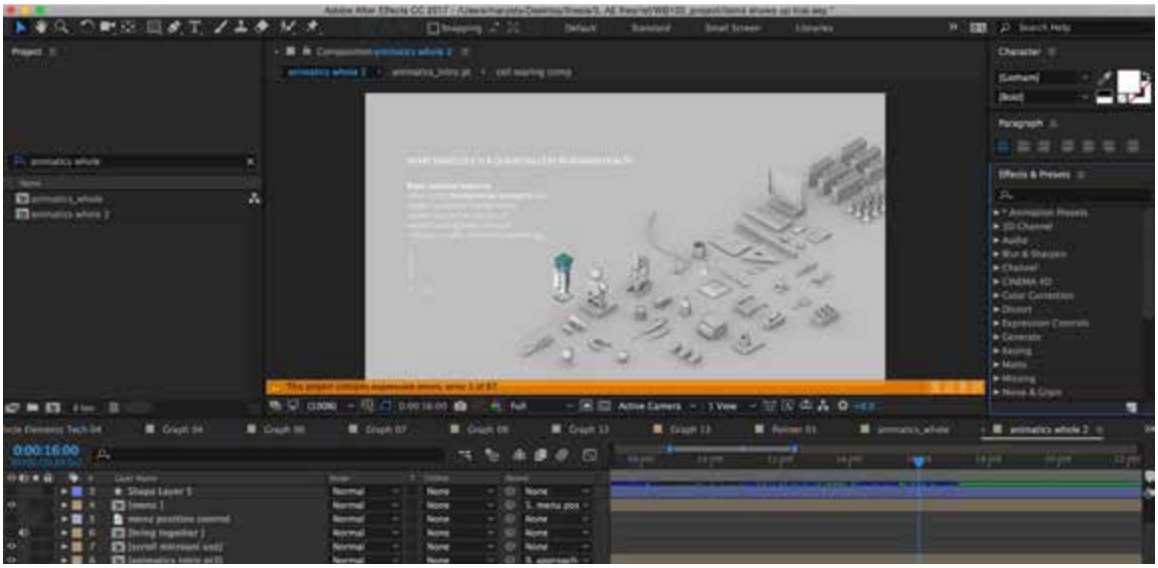


Figure 40. Example of the After Effects workstation. Text not intended to be read.

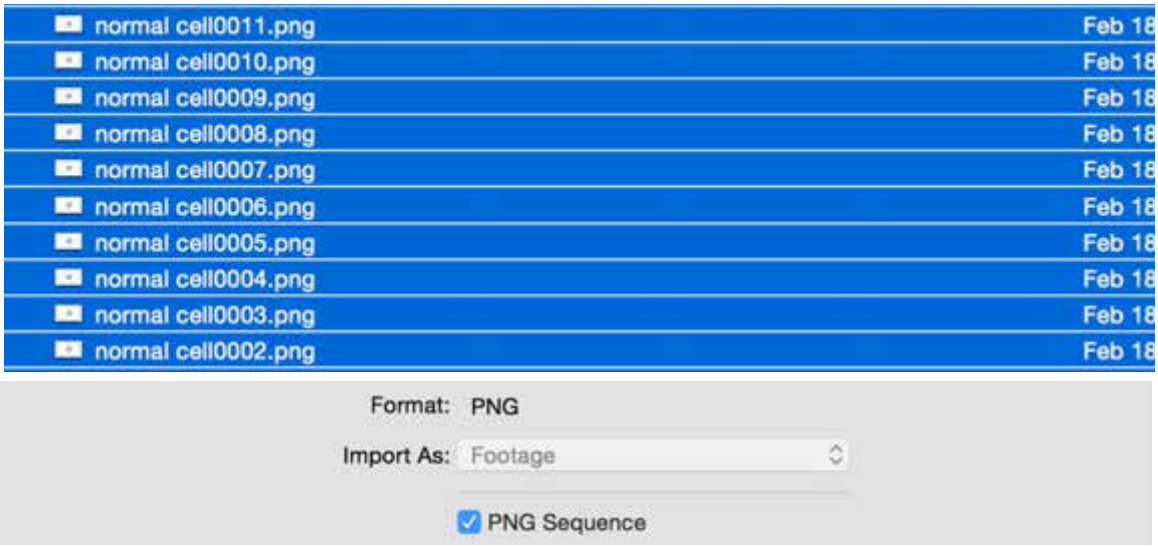


Figure 41. Import PNG Sequence. Animations rendered in C4D and exported as PNG Sequences.

Loop Animation with Time Remapping and After Effect Expression

Animations created in Cinema 4D were rendered with a limited number of frames in the form of PNG sequences. After Effects allows looping of these animations (**Fig. 42**).

PNG sequences imported into an After Effects composition show as an individual layer. Time Remapping can be activated by right clicking the layer > choose Time > Enable Time Remapping. This will add the Time Remap feature to the timeline. Alt click on the "clock" icon next to "Time Remap" opens the Expression menu > click the play button next to "Add:" > choose property > LoopOut > drag the end of the timeline to loop the animation for certain amount of time.

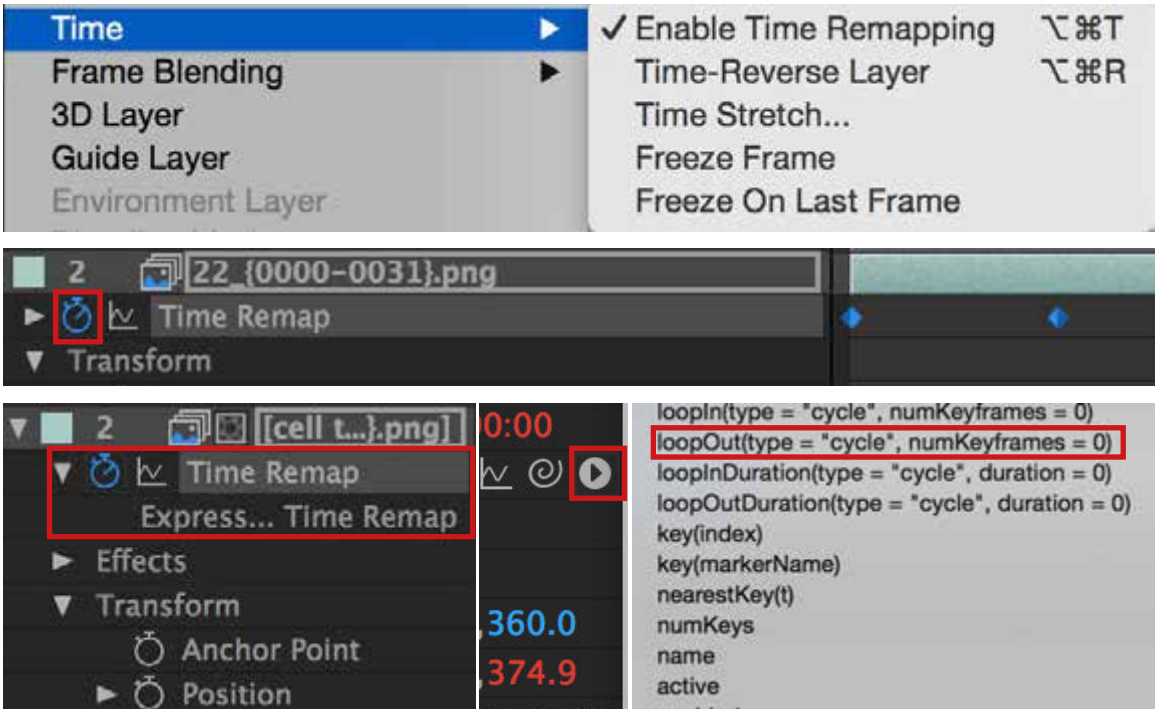


Figure 42. Loop animation. Time Remapping and Loop Out expression.

Test motions in KeyNote

Keynote was used to quickly test the effectiveness of text transitions and movement of the images, before proceeding to After Effects. Under the "Animate" tab, there are three types of object-based animation presets: "Build In," "Actions" and "Build Out.", and one set of slide-based animation, such as Magic Move (**Fig. 43**). "Move" (Action > Move) was applied to the images to achieve horizontal scrolling effect. "Dissolve" (Build In/ Build Out > Dissolve) was used to fade the paragraphs in and out. The animations were then arranged in a specific order by setting up the "Build Order" (**Fig. 44**).

Figure 43. Animate in Keynote. Animation Presets include Page Transitions, Build In, Action, Build Out.

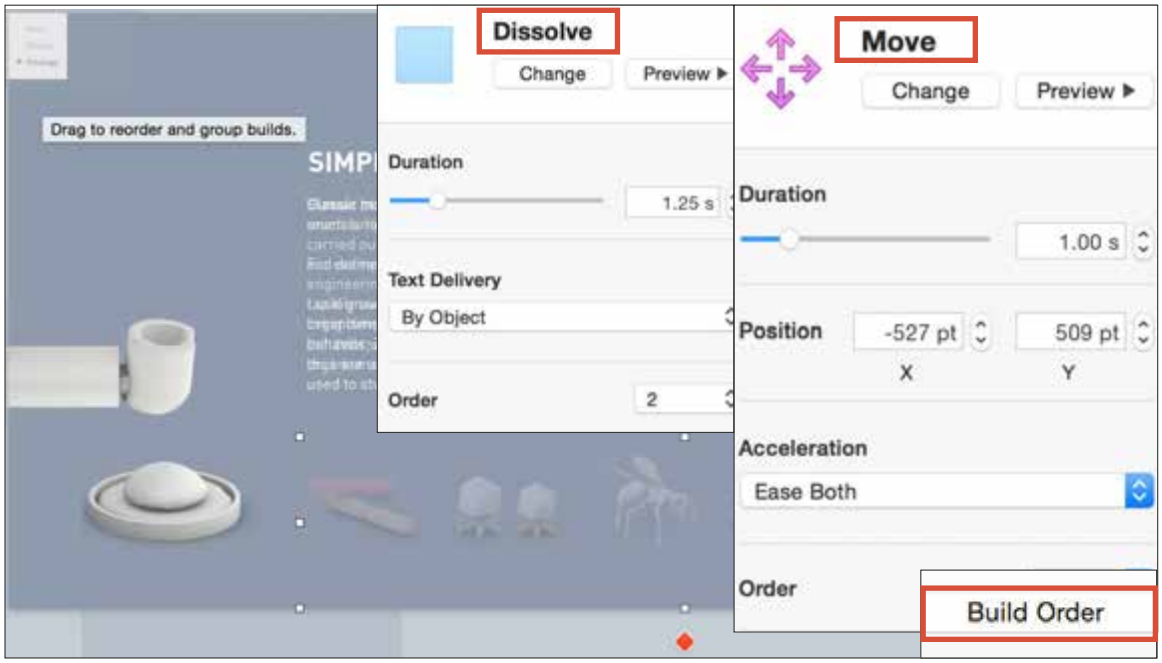


Figure 44. Example of Keynote interface. Not all text is intended to be read.

Scrolling Triggered Video Playback with JavaScripts

The final animated video was created based on feedback of the animatics. The video, audio and other related files were well-labelled and organized in a single folder. Pre-written JavaScript and HTML scripts were applied to the files, to control the progress of the video in response to "scrolling". This technique, called "scrolling triggered video playback", enables self-paced control of the video through scrolling up and down in the browser.

The alpha version of the codes, referred to as "Scrolleo" (Scrolling + Video) by the author, was created and shared by Mark Teater on CodePen and GitHub (**Fig. 45**). The codes were tested locally, customized and combined with HTML canvas animation and elements. JavaScript, HTML and CSS scripts are attached in the Appendix D and E, respectively.

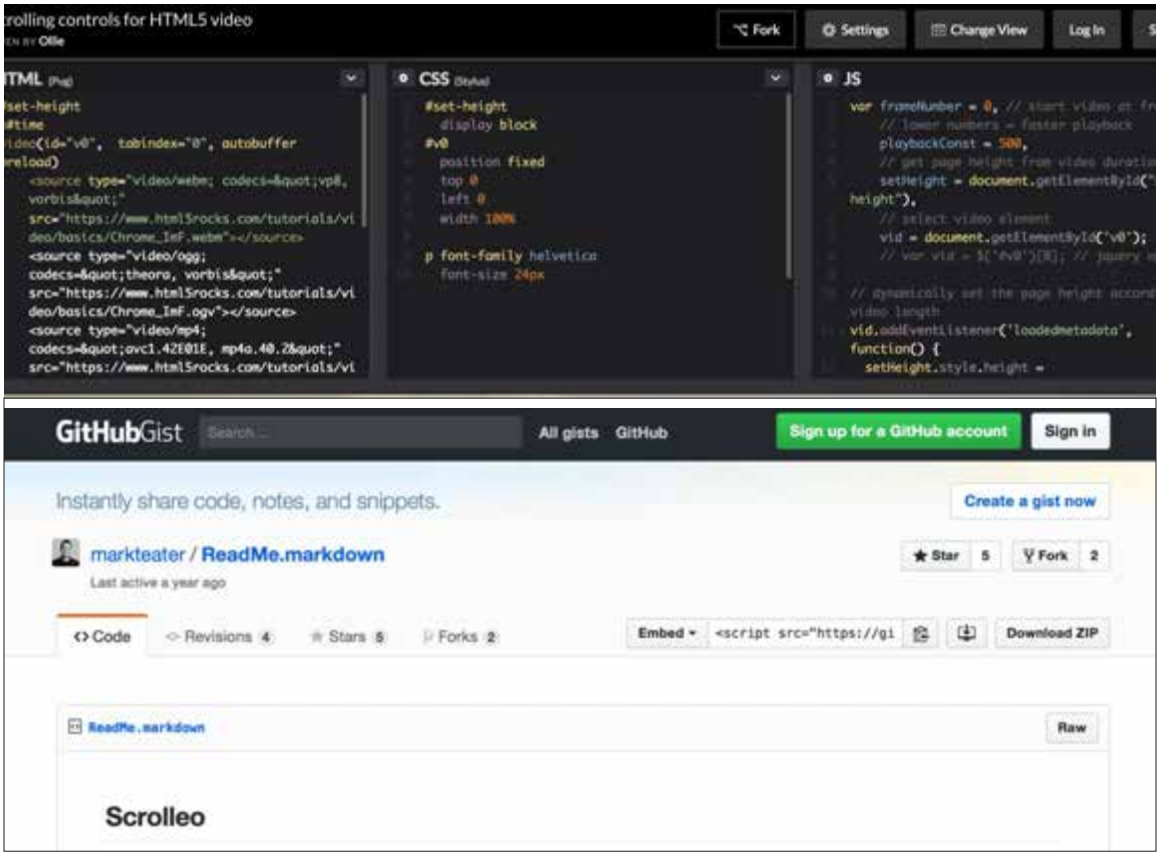


Figure 45. Example of CodePen and GitHub interfaces. The alpha version of Scrolleo was introduced and shared on these open sources by the author Mark Teater. Text not intended to be read.

The general mechanism (**Fig. 46**) of the script is to link the video duration (temporal measurement) into the document height (spatial measurement), using Javascript functions (document.height = Math.floor(videoDuration) * scrollScale + "px", scrollScale is a fixed factor that determines how many frames to play when scrolling once). When the scroll bar reaches a predetermined height, the browser obtains the scroll height, translates the height back to the temporal measurement, and returns the video current time. (Video.currentTime = (scrollHeight/ document Height) / scrollScale).

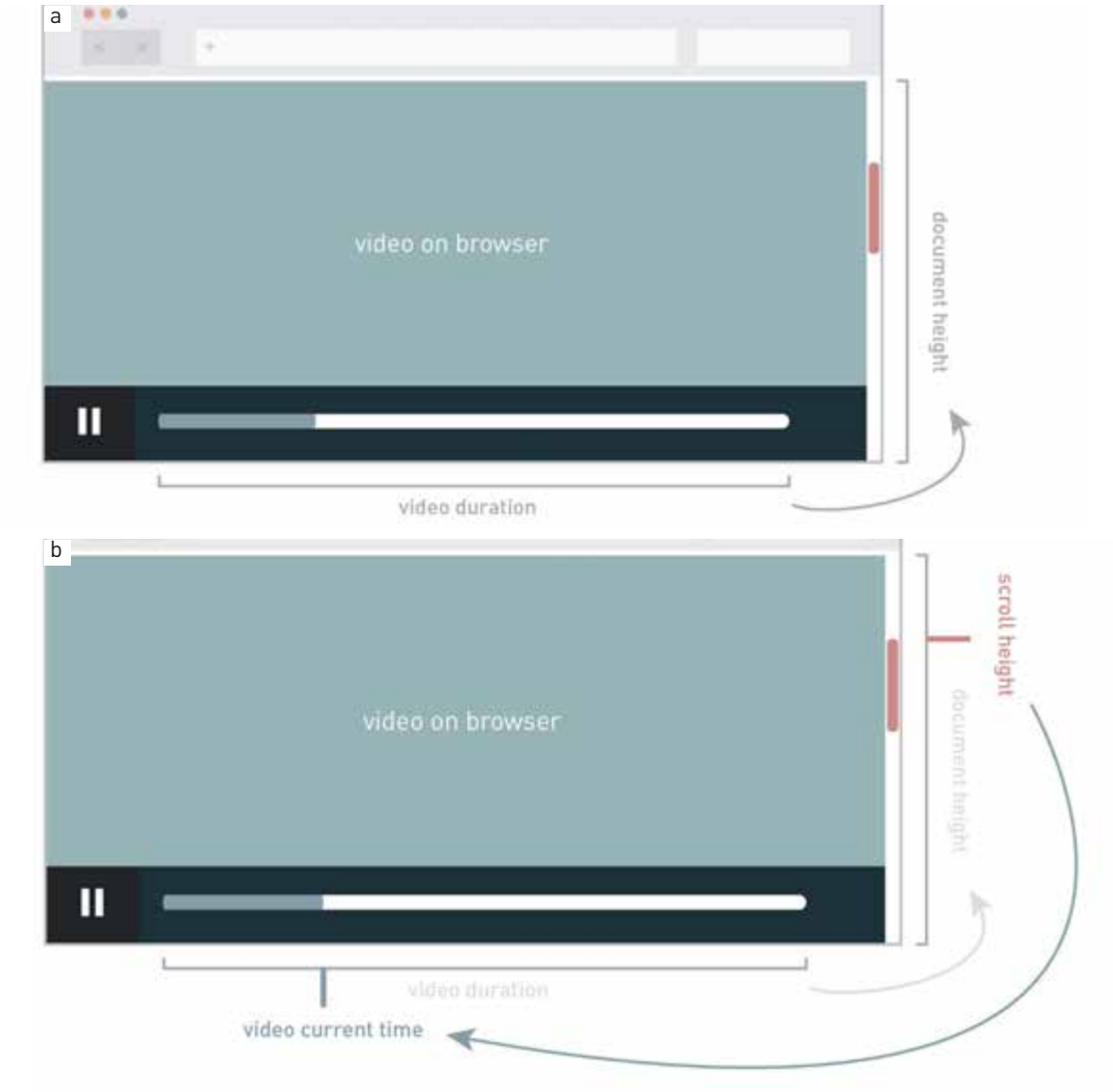


Figure 46. Javascript Mechanism. a, step 1. Conversion of the video duration into the document height. **b, step 2.** Translation of scroll height back to video current time.

Several other factors were taken into consideration to ensure a smooth scrolling experience:

(1) Format Conversion

The animated video exported from After Effects is a MOV file, which is not the most compatible format for browser-based presentation. Format Factory (**Fig. 47**) was used to convert the MOV file into an MP4 file. The MP4 video was then converted and compressed into Webm format, which compressed the video size by 10 times with only a slight compromise of the resolution.

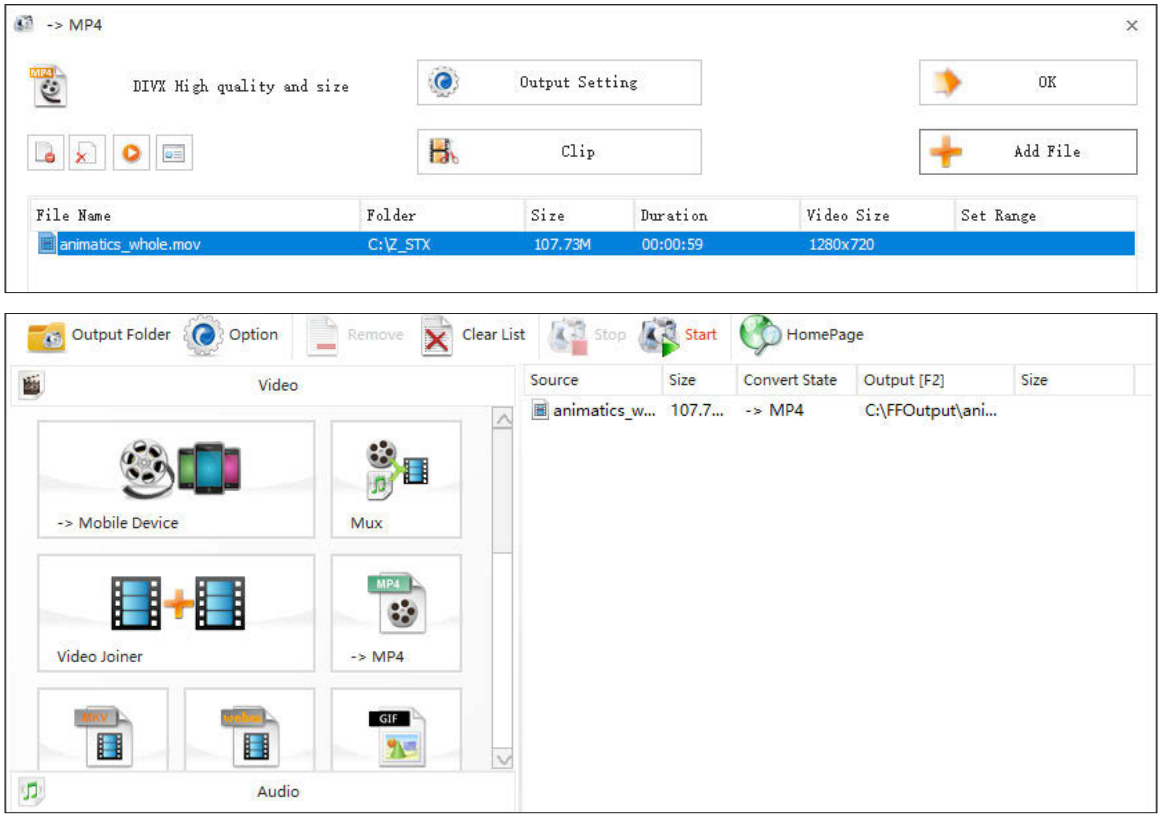


Figure 47. The interface of Format Factory. Not all text is intended to be read.

(2) Keyframe setting

To ensure that the scrolling playback is not choppy each frame must be set as an individual keyframe. This gives each frame equal weight and forces the browser to show every frame as scrolling, instead of skipping between keyframes that may be too far apart.

(3) Browser optimization

Various browsers have different rules to define property of HTML labels. Some consider that HTML header do not take space so the document height is determined by the Body. While others take all document elements into account. To ensure compatibility across different browsers, both rules were considered when calculating the document and window height (**Fig. 48**).

```
// get document height
function getDocumentTop() {
    var scrollTop = 0, bodyScrollTop = 0, documentScrollTop = 0; // different browsers
    if(document.body) {
        bodyScrollTop = document.body.scrollTop;
        }
    if(document.documentElement) {
        documentScrollTop = document.documentElement.scrollTop;
        }
    // console.log("==="+bodyScrollTop+"|"+documentScrollTop);
    scrollTop = (bodyScrollTop - documentScrollTop > 0) ? bodyScrollTop :  documentScrollTop;
    return scrollTop; // return the bigger value
}
// get window height
  function getWindowHeight() {
        var windowHeight = 0;
        if(document.compatMode == "CSS1Compat") {
            windowHeight = document.documentElement.clientHeight;
        } else {
            windowHeight = document.body.clientHeight;
            }
```

Figure 48. Section of the script. Compatibility across browsers was taken into account.

Design Concept

This web-based public outreach program developed during the course of the thesis communicates information about the critical role of fundamental research in human health. The thesis focuses on both written and artistic approaches of conveying advanced concepts. This includes the development of the word story, 3D models and animations, 2D motions, as well as user interface and experience design. An interactive website (**Fig. 49**) is under development to embrace the word story and artworks in a visually pleasant and easy-to-follow manner. The website will host five full-screen interactive videos to walk the audience through a storyline that helps communicate the concept, "what can fundamental research do for you?".

One key development of the program was the incorporation of a specific technique, namely "Scrolling Triggered Video Playback" into user interactive design. This JavaScript coded interactivity gives users full control over the progress of the animated video. The intuitive nature

Figure 49. An example of the user interface on the local browser and a list of the working files.
(video size: 1080 x 720; video frame rate 30 fps. video format: webm) Not all text is intended to be read.

of scrolling up and down prevents the audience from getting lost or being overwhelmed by buttons and hyperlinks while they are navigating through the site.

A second aspect of the program focuses on the consistency of the user interface design that is expressed across the following design attributes:

(1) **Color, size and shape**

This was achieved by first developing the color scheme (**Fig. 50**). The color scheme of the user interface was designed to be clean, calm and professional. Five main colors were chosen: blue as the background color; white with a silver tint as the main color for the 3D models, supplemented with red, yellow and green. Second, DIN Pro was chosen to be the typeface across the site. Font sizes of the title, body text, menu and page numbers were set up to build the hierarchy in reading and kept consistent throughout the program. Additionally, consistency of the design elements, such the thickness of the strokes, was paid attention.

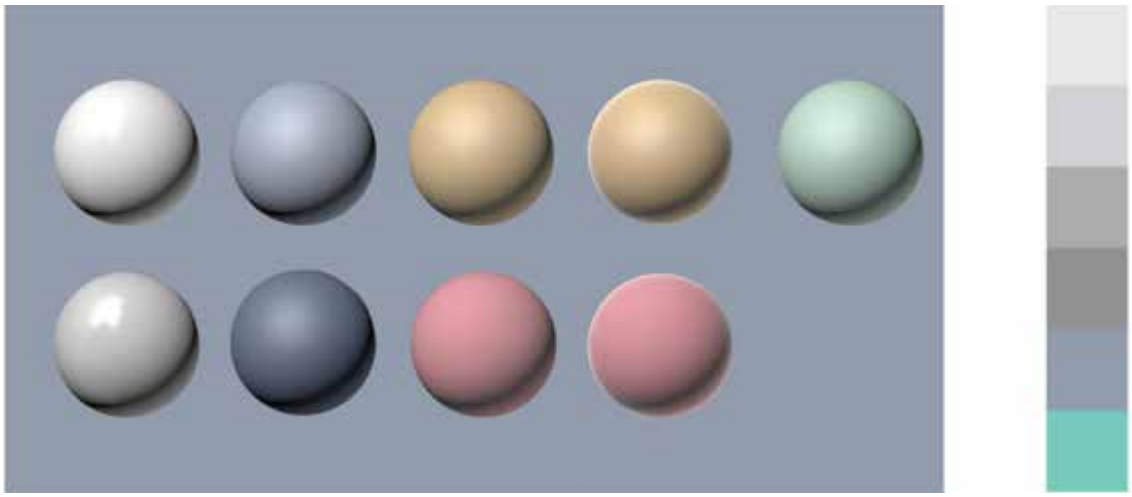


Figure 50. Color scheme. 3D and 2D color palettes.

(2) Content and Imagery

3D models, animations and 2D assets (**Fig 51-54**) have a stable and consistent style.

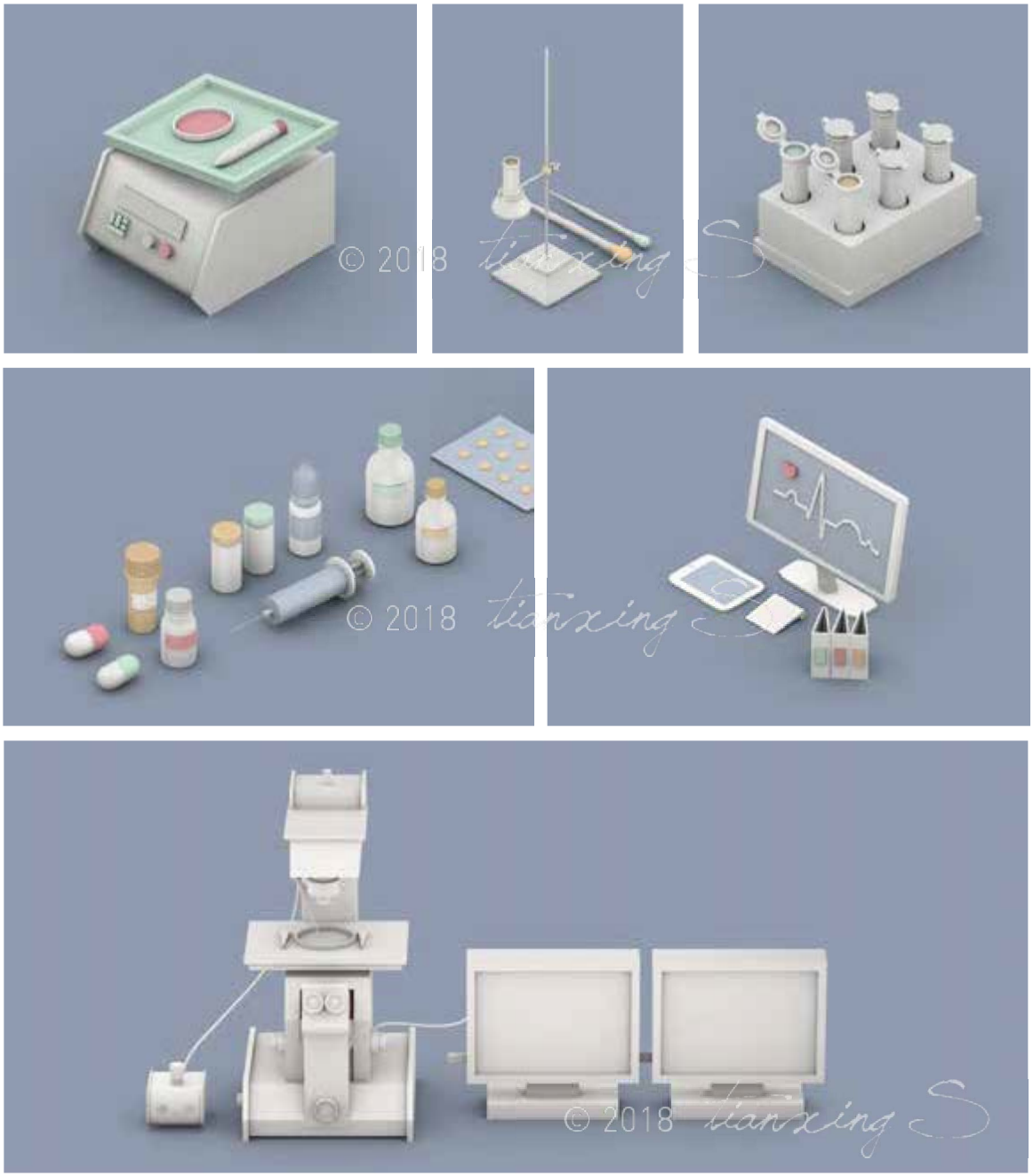


Figure 51. 3D assets 1. Research and medical devices.

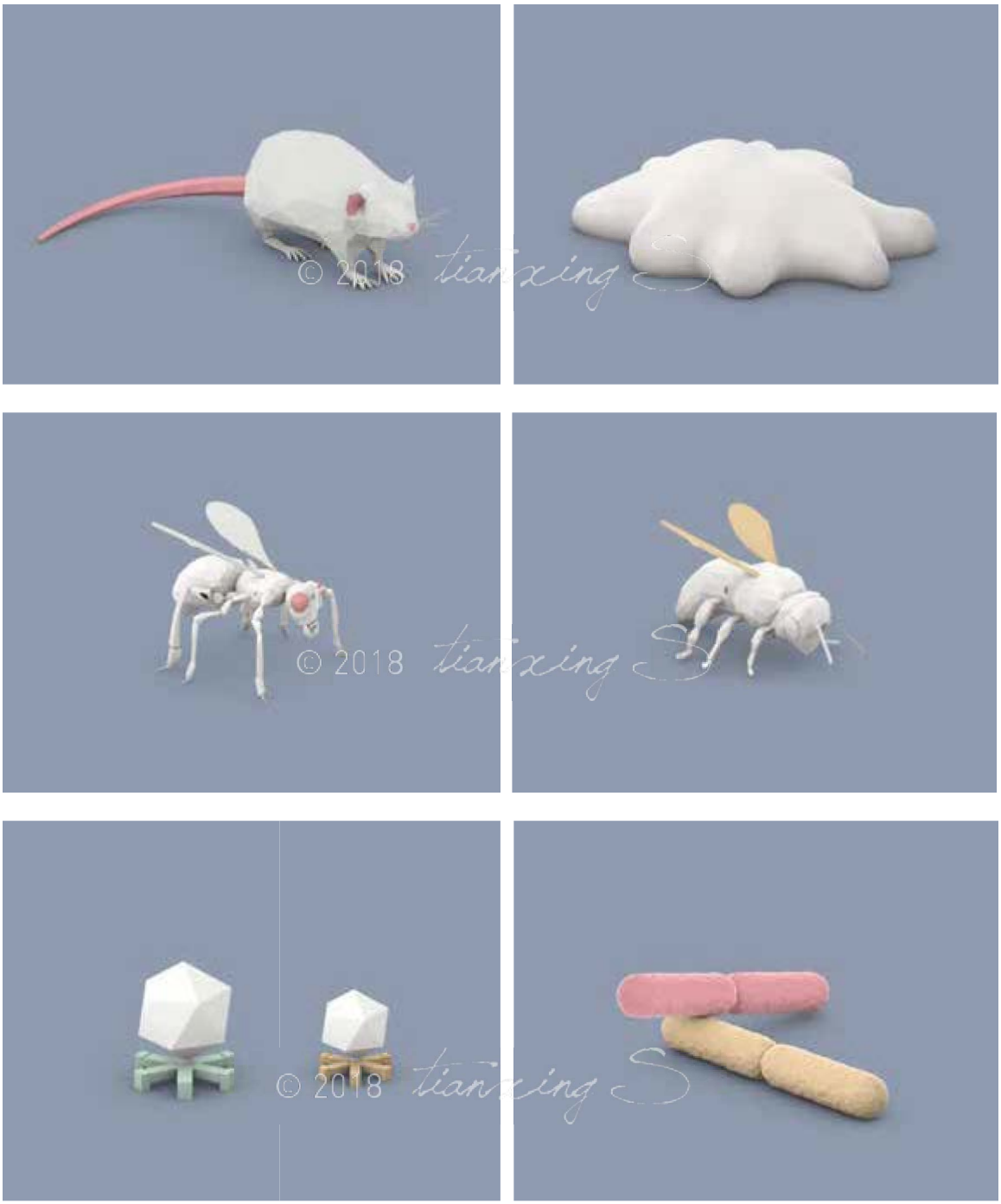


Figure 52. 3D assets 2. Research model organisms.

Figure 53. 3D assets 3. Research instruments.

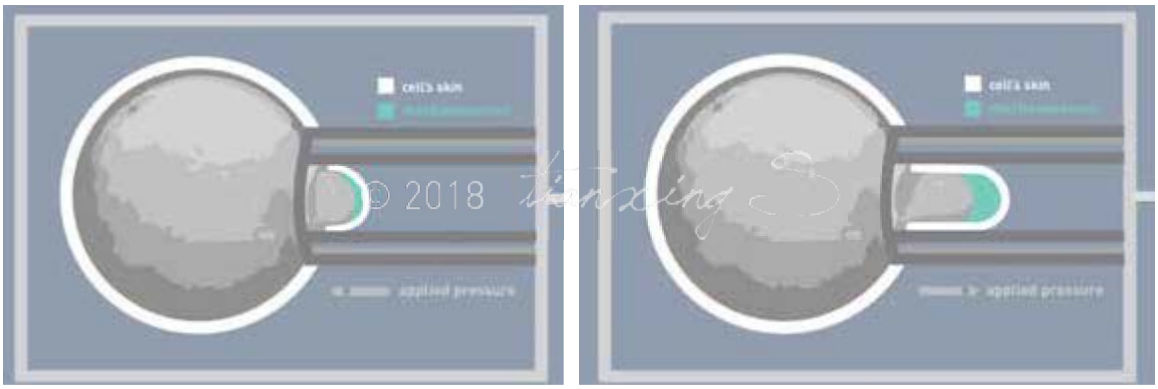


Figure 54. 2D art assets. 2D animation of Micropipette aspiration (MPA).

(3) Layout

Three master layouts were created for the compositions of the videos. The position and volume of the paragraph were designed based on the amount of written information to be presented.

Layout 1 Main page | Video 1: Intro part 1-2 (Fig. 55)

Background information on current health challenges and fundamental biomedical research is presented in short paragraphs at the upper left corner of the screen. The isometric design is intended to create a visual sense of the research world in a simplified and pleasant way.

Figure 55. Layout 1. Introduction part 1-2. Text not intended to be read.

Layout 2 Main page | Video 1: Intro part 3-4 (Fig. 56)

As more advanced concepts are introduced, such as the challenge in experimental design, the space taken by the imagery is reduced and positioned to the center, longer paragraphs are presented and placed under the imagery. It is designed to minimize distraction so that viewers could explore all the information by focusing on the center portion of the screen.

Figure 56. Layout 2. Introduction part 3-4. Text not intended to be read.

Layout 3 Child pages | Video 2-5: Research strategy 1-4 (Fig. 57)

Four research strategies are further explained through four videos on separated pages that are linked to the main page. The visual elements are further reduced in size and positioned to the lower one third of the screen, leaving more space for the word story. As users scroll, visuals move from right to left, introducing new elements to help explain the information.

Figure 57. Layout 3. Child page 1 "Simplify". Text not intended to be read.

(4) User interactive pattern

The interactive pattern (mostly scrolling) is kept simple and consistent throughout the site, guided with clear instructions (**Fig. 58**). The animated icon "scroll to explore" appears when the users are about to finish the current section. Underline indicates that the element is clickable. Page navigation elements, including page numbers, and a progress bar are presented at the same location across each page to indicate users about how much they have achieved and how much more to expect.

Figure 58. Instructions. Animated icon "Scroll to explore"; clickable "underline"; page navigation.

User Interface Design

Screen-captures of the user interface design can be found on the following pages (**Fig. 59 - 75**).

The texts in the images are not intended to be read.

Figure 59. Loading page design. Loop animation of amoeboid movement.

Figure 60. Landing page design. Opening: How does fundamental research help you?

Figure 61. Main page design 1. Introduction part 1: current health challenges. Noted that the text is not intended to be read.

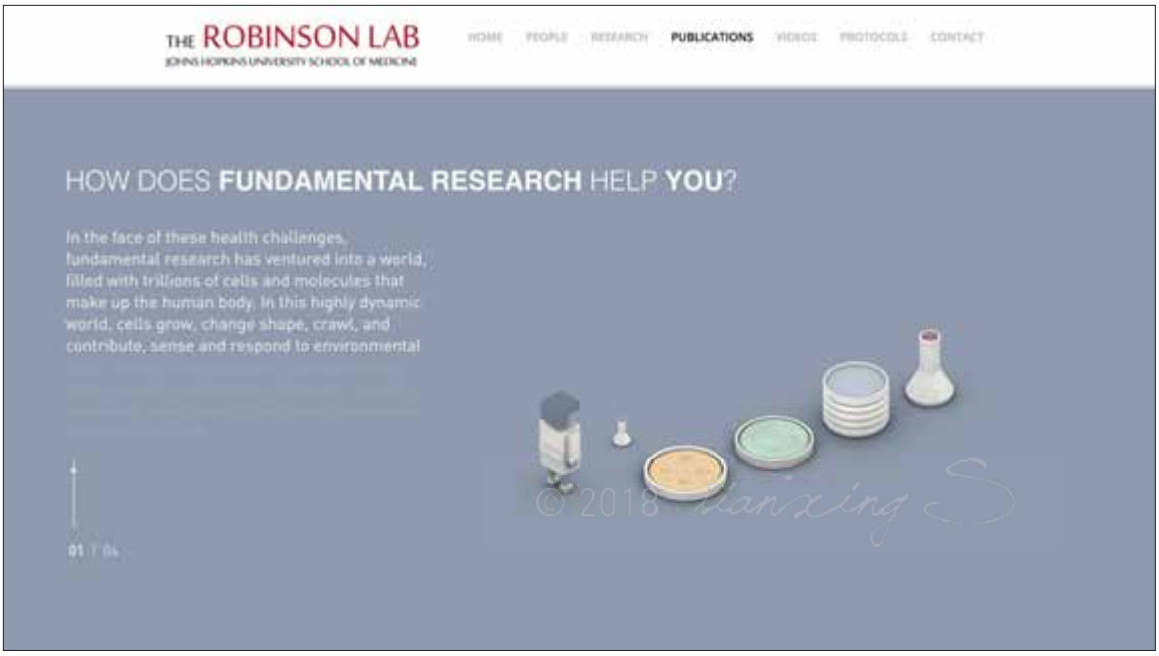


Figure 62. Main page design2. Introduction part 1: In the face of current health challenges, fundamental research has ventured into a highly dynamic world of cells and molecules that make up the human body. Noted that text included in the image is not intended to be read.

Figure 63. Main page design 3. Introduction part 1: While medical breakthroughs are made possible along the research process, researchers are poised to expand our understanding of the cellular and molecular behaviors involved in various diseases in order to create even better treatments. Noted that text included in the image is not intended to be read.

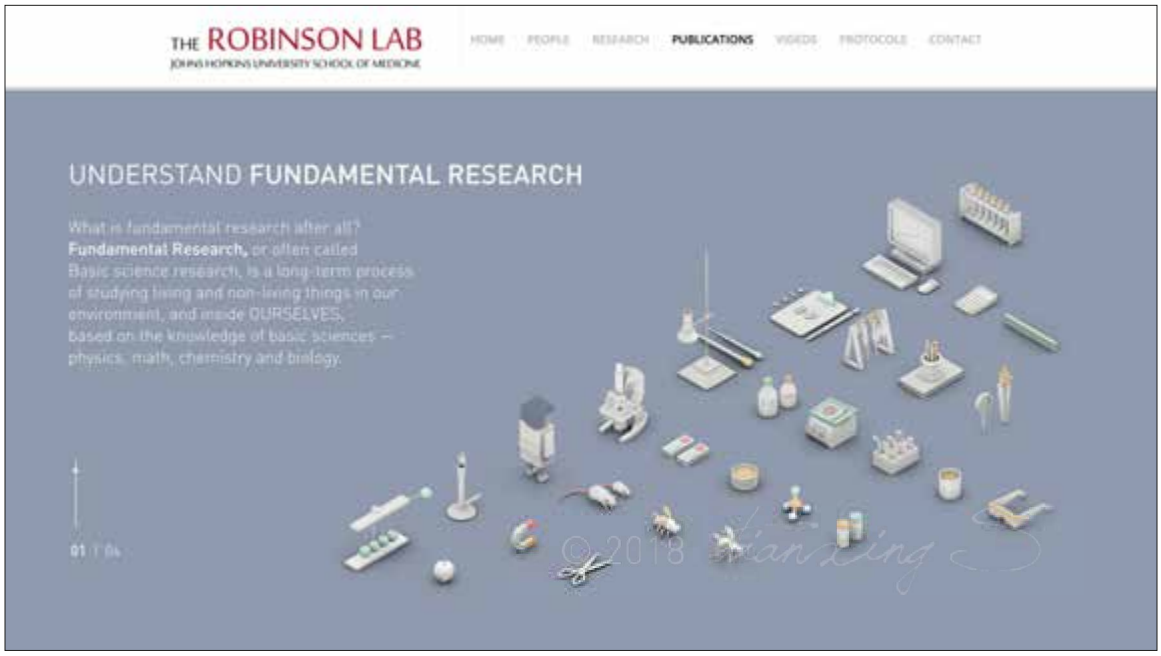


Figure 64. Main page design 4. Introduction part 2: what is fundamental research after all? Noted that text included in the image is not intended to be read.

Figure 65. Main page design 5. Introduction part 2: general flow of doing research. Noted that text included in the image is not intended to be read.

Figure 66. Main page design 6. Introduction part 3: There is still so much we do not know about various diseases like cancer, heart disease, COPD, and diabetes. Before we can cure diseases, researchers are seeking for answers to many basic questions, such as, why cells move? how do they communicate amongst themselves? The answers will lay the foundation for understanding biology of various illness. Noted that text included in the image is not intended to be read.

Figure 67. Main page design 7. Introduction part 3: Finding the answers to these basic questions, however, is greatly hindered by the extreme complexity of the human system. Direct experimental designs are not only difficult, but also time-consuming and economic-inefficient. Noted that text included in the image is not intended to be read.

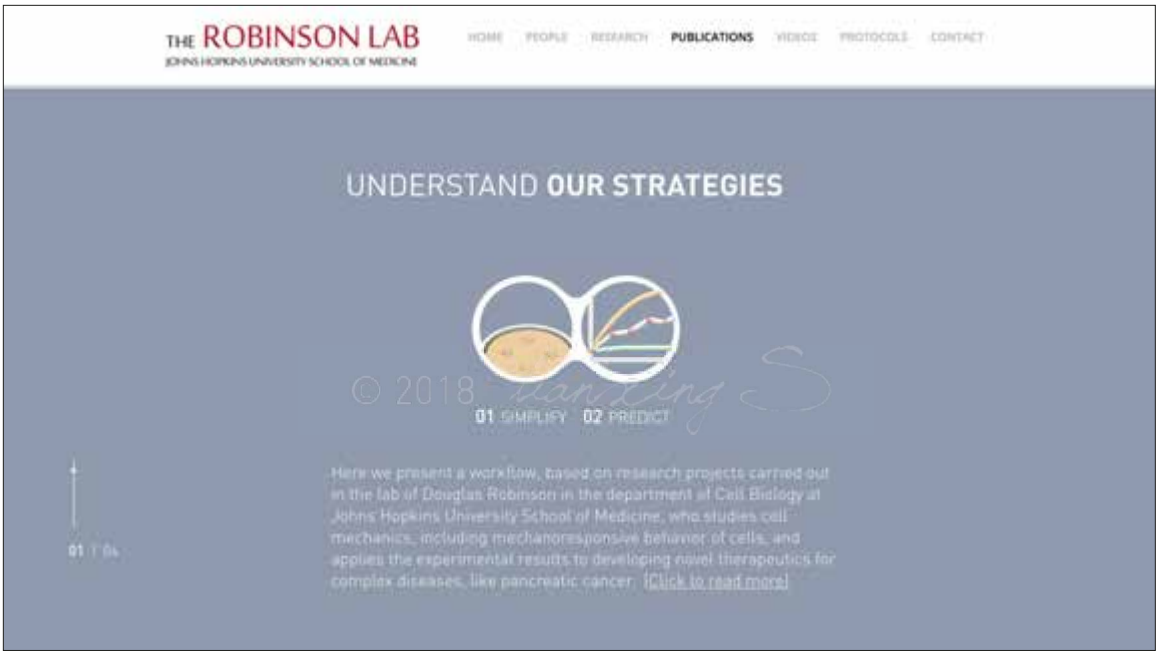


Figure 68. Main page design 8. Introduction part 4: to save time, materials and money, scientists have developed various strategies. Here we present a workflow based on research projects carried out in the Robinson Lab in the Department of Cell Biology at Johns Hopkins University School of Medicine. Noted that text included in the image is not intended to be read.

Figure 69. Main page design 9. Introduction part 4: the workflow is generalized into a series of four strategies, namely simplify, predict, test and screen. Users can click on each one to read more. Noted that text included in the image is not intended to be read.

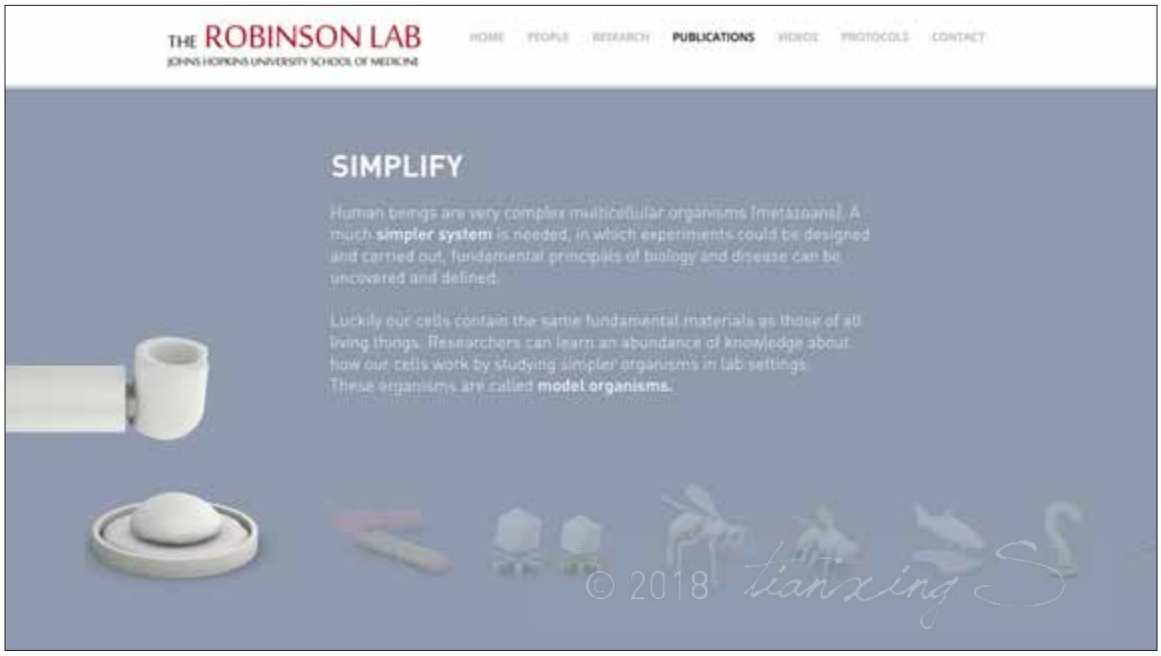


Figure 70. Child page design 1. Simplify: human beings are very complex organisms. Simpler model organisms are studied in lab settings, in which fundamental principles of biology and disease can be uncovered and defined. Noted that text included in the image is not intended to be read.

Figure 71. Child page design 2. Simplify: classic model organisms include E.coli, Phage, fruit fly, honeybee, zebrafish, worm and mouse. Noted that text included in the image is not intended to be read.

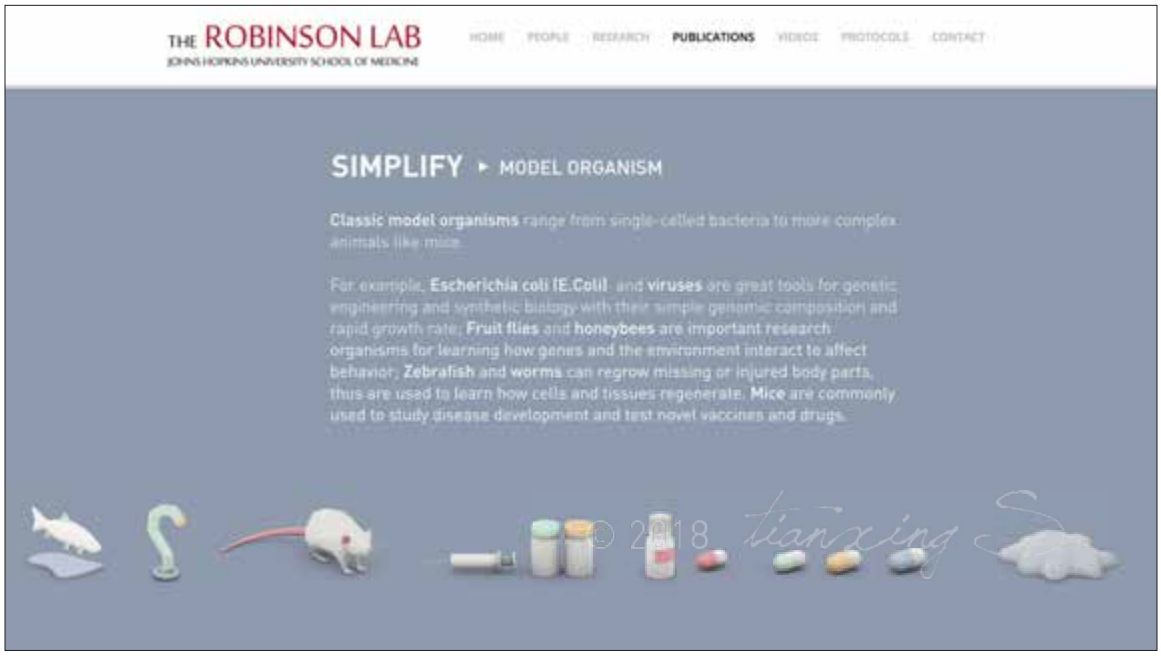


Figure 72. Child page design 3. Simplify: the end of "classic model organisms". Dictyostelium is about to show up. Noted that text included in the image is not intended to be read.

Figure 73. Child page design 4. Simplify: Common feature of Dictyostelium and its role in studying various human diseases. Noted that text included in the image is not intended to be read.

Figure 74. Child page design 5. Simplify: studies in Dictyostelium conducted in the Robinson Lab revealed cellular behavior and protein dynamics involved in cancer metastasis. Noted that text included in the image is not intended to be read.

Figure 75. Sticky footer design. Contact information, contact form and map. Noted that text included in the image is not intended to be read.

Asset Referral Information

The animated videos can be reviewed at:

http://robinsonlab.cellbio.jhmi.edu/videos

The scrolling video site can be accessed through:

http://marytianxing.com/#thesis

A copy of this thesis and all its assets is located in the Johns Hopkins University Department of Art as Applied to Medicine.

DISCUSSION

Fundamental research is a relatively abstract and complex process. The nature of the science itself can pose a major challenge for communication. Diversity in the ways in which people interpret information can add to the challenge. In order to create a successful public outreaching program, several strategies were employed and considerable thought was required to address the challenges of communicating and visualizing fundamental science.

Word Story Development

The development of Word Story, (information presented in the form of a story to help explain complex issues), is a method frequently used by science communicators. (Entwistle et al., 2011; Shaffer and Zikmund-Fisher, 2012). Word Story, sometimes referring to a narrative, can increase audience engagement with and attention to science communication, and be easier to remember and process relative to traditional forms of scientific communication, such as academic literature. (Bekker et al., 2013; Dahlstrom, 2014; Kanouse et al., 2016) The development of the Word Story is the very beginning and probably the most challenging part of the entire project. During this process, A few factors were taken into consideration.

(1) The extensive scientific terms were carefully translated into language the general public could understand or follow. For example, “cell cytokinesis” was replaced by “cell shape control”; “cell cortex” (the structure of the cell, referring to cell membrane and the cytoskeleton network just beneath the membrane) was replaced by “cell skin”. These wording changes were discussed with Dr. Robinson to ensure accuracy while minimizing the jargon.

(2) Since communication that considers people’s challenges with numeracy is generally more effective, (Peters et al., 2007), the numerical information was either coupled with visual

elements to help with the understanding or removed from the story entirely if doing so would not diminish the flow and accuracy of the content. For example, when explaining the use of computational modeling in simulating and predicting human systems, stylistic line graphs with a few dots were used to provide a general sense of statistical information, however, they did not include mathematical information that would require specific knowledge.

(3) The flow of the information was carefully designed and modified based on feedback from various sources, including faculty advisor David Rini, content preceptor Dr. Robinson and other non-scientists reviewers. Firstly, information was presented in small sections, which was intended to give user a break in between sections to process the new information. Second, each section, such as research strategies, was designed to have three layers of information, starting with a very general and brief description, followed by well-defined background information, and finally ending with specific examples.

Choice of Case Study

The study of cell mechanics in cancer treatment was chosen to be the case study to explain research concept and approach for several reasons. First, this research project integrates several subfields from cell biology, protein dynamics, to computational modeling and chemical biology. It follows a relatively linear workflow, which gives the audience a broad view of current biomedical research; Second, the study delivers the message to the audience that model organisms play a key role in fundamental research. The message provides answers to frequently asked questions, such as, why doing experiments in bacteria or animal species that are seemingly very irrelevant to human? Third, the study has great value in medicine and cancer therapy. Topics related to human health and disease prove to be powerful in drawing people's attention. Additionally, the study of cell cytokinesis and mechanosensing is an interesting topic not commonly covered in biology curricula. Though mitosis and cell division is often taught in

basic science education, cytokinesis and mechanosensing involve more advanced knowledge. Further, current approaches to cancer treatment focus on targeting signal transduction pathways. Cell mechanics offers an alternative approach to potential novel therapeutics.
Apart from the development of a narrative Word Story, a few other factors regarding the artistic style, user experience design, feedback collection were also carefully considered, as discussed below.

Artistic Style

(1) Isometric projection

Different from true perspectives, lines under isometric projection do not converge to a vanishing point but run in parallel. This method of visual representation of three dimensional objects is intended to provide the illusion of depth without distortion. Isometric projection is conventionally used by engineers, architects and technical illustrators for easier presentation and measurement of designed products. While the lack of foreshortening of the 3D objects provides a rather clean and consistent looking to the design. This technique, often combined with low-poly modeling (to be discussed later) became popular in the field of graphic and web design, as well as user interaction development in recent years.
In addition to the aesthetic value, the lack of distortion also makes it much easier for future adjustment to the design layout. Changes in scale and position of an object do not disrupt the visual projection of the entire scene, which accelerates the workflow to a great extent.
Both Adobe Illustrator and Cinema 4D (C4D) are commonly used for creating isometric designs. Compared to the process of scaling, sharing and rotating the shapes in Adobe Illustrator, the camera setting in C4D allows isometric projection rendered through the camera directly.

(2) Low-Poly modeling

3D models of lab instruments and research subject matters were created with a relatively small

number of polygons, to primarily reduce render time. Apart from working efficiency, models with low polygons can also have a desirable appearance. With compositions of basic geometry like cubes, cylinder, spheres and triangles, low-poly models offer a simple and clean aesthetic style, which is believed to be suitable in visualizing complex information.

User Interactive Experience: Scrolling

In computer displays, scrolling refers to sliding text, images or video across a monitor vertically or horizontally. "Scrolling" as a technique in user interactive development, does not change the layout of the text or imagery, but simply moves the user's view across the entire content. Users scroll down to reveal what is to be shown next and scroll up to review what has been displayed. This intuitive way of user interaction was incorporated in this thesis project to control the progress of the animated video, referring to a technique called "Scrolling Triggered Video Playback". The advantage and limitations of this technique are discussed below.

(1) Advantages of "Scrolling Triggered Video Playback"

Scrolling Triggered Video Site combines the advantages of traditional animation and web design. Users go through the website content as if they are watching a video. More importantly, they have full control over pacing based on how fast or slow they scroll.

The site supports a level of storytelling that cannot be accomplished with page-by-page navigation. With HTML5, Javascript, CSS3, and an animated video, a sophisticated story can be unfolded effectively using intuitive scrolling. "Scrolling up and down" controls "play", "pause" and "playback" of the video, which activates multi-plane animation, introduces new text and motion. This constant stimulation of changing elements instills a site with a film-like power that arouses curiosity, keeps users on-page and engaged longer. Additionally, the intuitive nature of scrolling-down prevents the audience from being overwhelmed by the navigation buttons, thereby promoting effective interactivity and guiding users to discover additional content.

Scrolling triggered Video Playback technique potentially presents a streamlined workflow in web development for both designers and web developers. In general, designers and web developers work in different ways to meet a variety of goals. Designers come up with designs of front-ends visual presentations and communicate the ideas with prototypes. Web developers then re-create the visual effects based on these prototypes using back-ends coding, allowing computers to calculate and respond to users' interactions. Scrolling Triggered Video Playback allows partial skip of this re-creating process. As long as the video is well designed and created, it can be displayed on an HTML canvas directly and controlled by pre-written JavaScript. Other functional elements, such as buttons or links can be added on to multiple HTML layers. The set of JavaScript, HTML and CSS documents provide a framework that can be reused for future development of a Scrolling Triggered Video sites. Any video can be placed and controlled using the same framework. This technique also makes future edits of the site much easier, which is particularly important for a public outreaching program. Changes to the design and content are required throughout the development and upon publication, based on user feedbacks and comments. These changes can be easily made in animation programs, such as Adobe After Effects to create a new version of the video. The old version could be easily replaced by changing the file name in JavaScript coding. No additional edits in HTML and CSS are needed.It is important to note that this scrolling feature functions differently on different browsers. Scrolling currently works on Safari, but appears choppy on Chrome. Further analysis and testing of the codes is ongoing.

(2) Potential limitations

First, with complex content, audiences might miss the big picture while scrolling down and going deeper to explore more detailed information. To avoid this problem, the site is composed of a main scrolling page that ends with a big picture and link to four sub-pages that provide more detailed information. Audiences can easily go back to the big picture wherever they are in the process. Additionally, special consideration was given to the navigation icons so users are

able to maintain a sense of where they are in the site and how much more to expect. Second, even though Scrolling site appears to be a popular trend in interactive design, it remains as a revolutionary user experience to some extent, compared to conventional "clicking". However, big brands like Nike, Sony and Apple have incorporated this into their web design as an eye-catching marketing tool that has proven to be very successful. I believe the communication of fundamental science could also benefit largely from this technique, as long as instructional graphic elements are clearly shown on the screen to guide the users.

Developing a Mechanism for Receiving Timely Feedback

Collecting timely feedback from actual users during and after the project development is essential for creating a public outreaching program. These feedbacks prove to be helpful in identifying potential problems, making adjustments, and measuring the success. Various ways of presenting ideas and receiving feedback were explored during the course of the project.

(1) Word Story combined with wireframes were firstly brought to the brain-storming sessions and follow-up meetings to show the framework of the program. Several versions of wireframe could be efficiently created for multiple rounds of feedback collection at initial stage of the project development.

(2) Animated prototype or animatics were shown to art advisor in the middle of the user interface design. Problems in visual presentations were directly exposed, including the timing and speed of the transitions, the amount of motions shown on the screen at the same time, and the effectiveness of using certain animations to explain the information.
Adobe After Effects (AE) and Keynote were used for creating the animated prototype. AE provides flexible and powerful functions to animate page transitions and motions. While creating animations in AE requires certain amount of time to test various parameter settings and keyframes. Keynote or MS Powerpoint, on the other hand, can be used to quickly test a rough

idea with the built-in animation presets. It is straight to the point — there is no code, timelines with keyframes or complicated functionality. Rapid and high-fidelity transitions and movements can be created and tested. The combination of the two programs were used to accelerate the workflow.

(3) Screen captures of the final user interface designs and rendered animations were shared with content and art advisors, as well as non-science viewers including family members and friends. Informal surveys were conducted to measure the effectiveness of the program. One major comment was that the original opening was probably too long, thus not strong enough. The story included in the opening was then replaced with one question "How does fundamental research help you?" to draw people's attention, since audience would probably show more interests in content that is directly relevant to their life.

(4) Contact forms will be included on the actual website. This allows long-term communication with the users. Future adjustment to the content and the design will be made according to their comments.

Appendix A: Informal Discussion List

From Fundamental Discovery to Human Health:

1.1 understanding basic science

- what is basic science
- what is basic science research
- why it is so important

1.2 Understanding research background

- what is Cell cytokinesis
- what is Cellular Mechanosensing
- how is cellular mechanosensing related to human health/ diseases

1.3 Understanding research concepts and process

a. experimental approach in model organisms:

- What are model organisms?
- Why are model organisms useful for fundamental research?
- How has work with research model organisms influenced human health?

b. from experimental to computational:

- what is computational modeling?
- How are computer models used to facilitate discovery?
- How can computational modeling improve biomedical research?
- Can computer models replace research organisms?

c. from theoretical models to human system:

- what are human-derived cells?
- how are human-derived cells important as vitro models in medicine?

- what do these cell lines tell us (in pancreatic cancer research)?

- what is immunohistochemistry?

- What information does immunohistochemistry provide to help understand human tissue?

d. from human system to therapeutic targets (compound screening):

- what is live cell high-throughput Screening?

- what have been discovered? (4-HAP treatment)

1.4 - Who funds basic research?

- How does basics research costs compared to total health care costs?

- What is the role of are basic research in improving health?

- Do we have evidence that research & development helps our economy?

Appendix B: Word Story

LANDING

How does fundamental research help you? (Scroll to explore)

INTRODUCTION

The population is aging, pathogens are spreading, and the demands on healthcare are increasing. Ebola, AIDS, and Influenza have dominated the headlines. Meanwhile, many of the complex diseases, like cancer, heart and lung disease, and diabetes, were once thought to be the "natural consequence of aging". However, these health problems result from the accumulated dysfunctions of cells and molecules. If scientists can uncover the basic mechanisms of these diseases, we will be able to solve them.

In the face of these health challenges, fundamental research has ventured into a world, filled with trillions of cells and molecules that make up the human body. In this highly dynamic world, cells grow, change shape, crawl, and contribute, sense and respond to environmental cues. Cellular molecules are constantly being made, moved, and modified. Although cells are constantly trying to get things right, sometimes mistakes are made.

Decades of fundamental studies are revealing clues about how these micro-level processes affect human health and how to repair them. Medical breakthroughs are made possible along the process. While many novel medicines, vaccines, and therapies have been developed, we are poised to expand our understanding of these cellular and molecular behaviors in order to create even better treatments.

Understand Fundamental Research

What is fundamental research after all?

Fundamental Research, or often called Basic science research, is a long-term process of studying living and non-living things in our environment, and inside OURSELVES, based on the

knowledge of basic sciences — physics, math, chemistry and biology.

The process we take part in is sophisticated and adventurous. Along this winding trail, we generate hypothesis, observe, test, measure, analyze and repeat.

(Keep Scrolling)

Understand the Complexity

Facing the unknown and uncertainties, we ask many basic questions: why cells move? how do they move? how do they communicate amongst themselves? All of these basic questions fall into three categories: (1) how do things function normally? (2) what would happen if the system breaks? (3) how to fix it?

Finding the answers to these basic questions, however, is greatly hindered by the extreme complexity of substantial molecules and cells of the human body. Direct experimental designs in human cells and tissues are not only difficult, but also time-consuming and economic-inefficient. To save time, money and materials, we have been seeking for simpler systems in which fundamental principles of biology and disease could be uncovered and defined.

Here we present a workflow, based on research projects carried out in the lab of Douglas Robinson in the department of Cell Biology at Johns Hopkins University School of Medicine.

The Robinson Lab studies cell mechanics, including mechano-responsive behavior of cells, and applies the concepts they are learning to developing novel therapeutics for complex diseases, such as cancer and chronic obstructive pulmonary diseases (COPD). (Click to read more)

RESEARCH STRATEGIES

01 SIMPLIFY

Human beings are very complex multicellular organisms (metazoans). A much simpler system is needed, in which experiments could be designed and carried out, fundamental principals of biology and disease can be uncovered and defined.

Luckily our cells contain the same fundamental materials as those of all living things.

Researchers can learn an abundance of knowledge about how our cells work by studying simpler organisms in lab settings. These organisms are called model organisms.

Simplify > Model organisms

Classic model organisms range from single-celled bacteria to more complex animals like mice. For example, *Escherichia coli* (E.coli) and viruses are great tools for genetic engineering and synthetic biology with their simple genomic composition and rapid growth rate. Fruit flies and honeybees and important research organisms for learning how genes and the environment interact to affect behavior. Zebrafish and worms can regrow missing or injured body parts, thus are used to learn how cells and tissues regenerate. Mice are commonly used to study disease development and test novel therapy.

Simplify > Model organisms > Dictyostelium

Dictyostelium discoideum (a.k.a. Dicty), a type of amoebozoan is a relatively recent addition to the list of model organisms for fundamental research. Dicty has proven to be a very effective tool in studying human cell behaviors. Living most of its life as a single, free-living amoeba consuming bacteria, its flexible plasma membrane without a rigid cell wall permits it to be highly motile, similar to human leukocytes. When it runs out of food, these free-living cells then join up and cooperate like an intelligent multicellular organism, forming many structures found in multicellular organisms such as epithelial tissues. Thus, these behaviors capture many of those presented by human cells and tissues. Moreover, the 34 Mb genome of Dicty contains many genes that are homologous to those in higher eukaryotes, including humans. These genes are either absent or are less accessible in other model organisms.

Addition to the behavior that capture a lot of attributes human cell have, Dicty also shows the common features of a model organism — can be rapidly grown to high cell densities in an inexpensive medium and easily observed under all forms of microscopy. Further, Dicty cells are easily studied biophysically. For mechanical studies, one common method is micropipette

aspiration (MPA). A small diameter glass pipet is brought into contact with the Dicty cell. A known suction pressure is then applied within the pipette, causing an aspiration of the cell into the pipette. By measuring the length of aspiration, several important cell mechanical properties, including cortical tension can be calculated. Cell deformability, in turn could be analyzed.

The combination of fluorescence microscopy and MPA enables high quality visualization of molecular components, including various proteins, during the process of cell shape change, as presented in the study of cell shape control at the Robinson Lab. Their studies in Dicty cells have revealed fundamental concepts. First, cell shape is maintained by a dynamic network of specific cytoskeletal proteins that interact tightly with the cell membrane. Second, within this network, a specific subset of cytoskeletal proteins sense and respond to mechanical stimuli and trigger subsequent cell shape change. This property is called mechanoresponsiveness, and these proteins are often referred to mechanoresponsive or mechanosensitive. These proteins are also critical components in cell movement and deformation, and are coordinated through a mechanical and biochemical feedback system. Third, if the expression of these proteins becomes abnormal, generally elevated, this leads to disrupted cell shape changes, movement, and mechanoresponsive. In cancer, this imbalance at protein level and migration at cell level could mutually reinforce each other to aggravate cancer metastasis.

02 PREDICT

Because of the considerable amount of sister proteins (or paralogs - proteins share the same origin) in human system that do not exist in Dicty cells (the Dicty genome is more streamlined), and the wide range of proteins in general, experimental results from these model organisms are still inconclusive in identifying the proteins that plays the role in human health and diseases. Computational Modeling, therefore, helps bridge the gap.

Predict > Computational Modeling

Computational Modeling is the use of math, physics and computer science to generate physical theories from experimental datasets. The power of computational modeling is that it allows scientists and engineers to simulate variations more efficiently by computer, saving time, money, and materials. The results of simulation help researchers make predictions about what will happen in the real system, most likely to develop further experimental design in human system.

Predict > Computational Modeling > Force-Dependent Model Predicts Mechanosensitivity

Myosins are a superfamily of motor proteins, well known for their roles in a wide range of cell motility processes. Studies in Dicty show that Myosin II is one of the mechanoresponsive proteins within the network of cytoskeleton, involved in cell shape maintenance and changes, as mentioned above. The three paralogs in human cells, namely Myosin IIA, IIB and IIC, were suspected to share the same property. Likewise, other mechanoresponsive proteins discovered in Dicty, such as alpha-actinin (ACTN) and Filamin, also have several sister proteins in human cells, which were also possibly to be utilized by cancer cells to achieve deformation and migration. In order to analyze the similarity and differences between these sister proteins in human cells and the homologous protein in Dicty, computer models were developed from experimental datasets generated from comprehensive investigation of Dicty, during which digital imaging, math, physics, and computer science were involved. The models allowed researchers to simulate the dynamics of sister proteins in human system. The statistical results of these simulations helped researchers predict several proteins attributes in human cells, such as mechanosensivity, reaction rate and localization patterns under different levels of mechanical stimulation. For instance, one of the simulation results suggested that under external mechanical stimulation, ACTN4 (one of the alpha-actinin paralogs) increased in intensity while ACTN1 did not, which indicated that ACTN4, but not ACTN1, was mechanoresponsive. The predictive power of the computational models greatly narrows the

range of molecular components to be tested in human cells and tissues, as well as the scope of the experimental design. These models, therefore, are very helpful tools in translating experimental results from model organisms to human systems.

03 TEST

With the guide of the computational predictions, experimental designs in human systems become more straightforward. Human derived cells and tissues were utilized at this point to test if the simulation correctly predicted the cell and protein behaviors.

Test > Human derived cells

Human derived cells are cells taken from human bodies, isolated and cultured in the laboratory under specific nutrients and space. Although they are removed from their normal context in human tissues, they still provide an invaluable tool for deciphering human disease relevant biology. Isolated cells allow for the examination of stepwise alterations in the structural and genetic makeup of the cell under controlled environments. However, many of these controlled environmental conditions include scenarios that reconstitute conditions the cells experience in normal tissue context. This ability to reconstitute defined tissue contexts with well-defined cells is especially valuable for studying complex tissues such as the pancreas, which is composed of various cell types and where in vivo examination of individual cells would be difficult. Further, the reconstituted tissue-like environments also allow for the ability to probe the cells and tissues, for example for mechanical studies.

Test > Human derived cells > Human Pancreatic Ductal Epithelial Cells & Pancreatic Adenocarcinoma-Derived Cells

In studies carried out in the Robinson Lab, several human-derived cells were investigated, to determine if the computational prediction of the mechanoresponsive property of the sister proteins in the human system is correct. These cell lines include immortalized Human Pancreatic Ductal Epithelial cells (HPDE), stage II pancreatic adenocarcinoma-derived cells

(Panc10.05), stage IV ascites-metastasis-derived cells (AsPC-1). HPDE cells are also used as a near normal pancreatic ductal epithelial cell comparator, while the others represent cancer cells in different disease states. In these cells, the targeted proteins were labeled with fluorescent proteins. Similar to the study of cell mechanics in Dicty, micropipette aspiration (MPA) was used to apply the external mechanical stimulation. The localization and concentration of the labelled proteins in response to applied external stress were measured. The experimental results were consistent with computational simulations, which confirmed the mechanoresponsive property of several previously suspected proteins, including Myosin IIC and ACTN4. The results also reflected the active involvement of these proteins in the process of cell shape change in both normal and cancer cells. Furthermore, cancer cells displayed higher level of cell deformation compared to the control group, as well as higher concentration of these proteins at the sites of deformation. This positive correlation between cell deformability and mechanoresponsive protein level in human derived cells highly suggested that mechanoresponsive proteins might be harnessed by cancer cells, leading to altered cell shape control and cell motility.

Test > Human Tissue

Patients' tissues are samples taken directly from patients during surgical resection to remove the patient's tumors (with patient consent). These samples provide direct information about disease states and are used to test whether discoveries in model organisms and human-derived cells are consistent with real-life situations.

Test > Human Tissue > PDAC Tissue Sample

To test if these mechanosensory proteins, such as Myosin IIC, were over produced in pancreatic cancer, tissue samples from PDAC patients were collected. Testing was achieved by using immunohistochemistry (antigen-antibody and tissue-based reaction), a method of tissue imaging. Secondary antibodies coupled with horse radish peroxidase (HRP) were applied

to the tissue slides followed by the chromagen DAB with which the HRP reacts to create a brown color. Where the tissue turns brown reflects where the protein is found, and protein concentration is represented by the intensity of the pigments. The resulting images observed under light microscope indicate that Myosin IIC and other mechanosensory proteins were highly up-regulated in the pancreatic ductal adenocarcinoma of patients, compared to normal tissues. The level of up-regulation is positively correlated to the stage of pancreatic cancer, further confirming that these mechanosensory proteins are critical components of cancer cell shape change and migration. Hence, these proteins might be potential therapeutic targets in reducing cancer metastasis.

04 SCREEN

The experimental results from both model and human systems suggest that one rational therapeutic approach is to correct tumor cell behavior by reducing cell deformation (in other word, increasing cell stiffness), which would in turn, reduce metastatic potential of cancer. This could be achieved by interfering with the mechanosensitive proteins like Myosin IIC, using small-modulators (small compounds).

Screen > High-Throughput Chemical Screening System

To seek for effective small compounds, an in vivo, high-throughput, chemical screening system was developed. This system enables the efficient discovery of possible drug precursors. Large numbers of compounds from compound libraries were added to and interact with cells in thousands of reacting wells. Sensitive detectors and data processing software made it possible to accurately pick up these potential compounds based on their ability to inhibit cell shape change

Screen > High-Throughput Chemical Screening System > 4-HAP

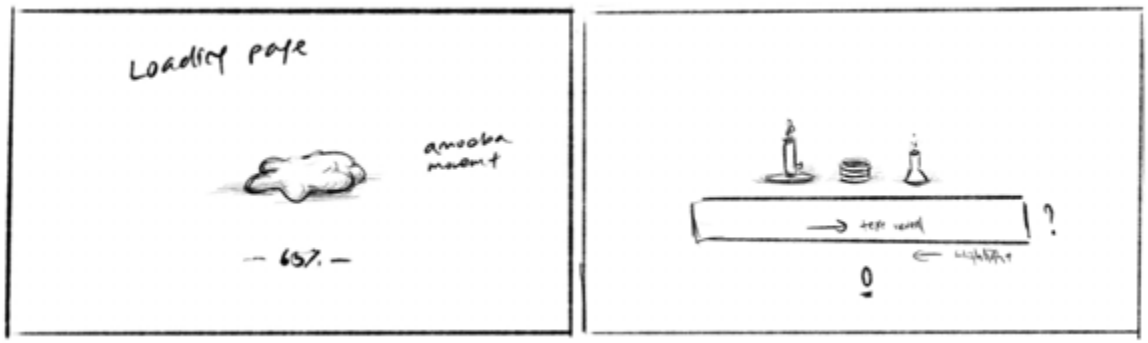
A small compound, 4-hydroxyacetophenone (4-HAP) was characterized by the Robinson Lab during the screening process. 4-HAP reduces cell deformation by forcing Myosin II to re-localize

along the cell skin (cell cortex). Such re-localization of mechanosensitive proteins increases cellular cortical tension and subsequent cell stiffness. In a mouse liver metastasis model, 4-HAP treatment reduced the metastasis of pancreatic tumors to liver, in comparison with the control group.

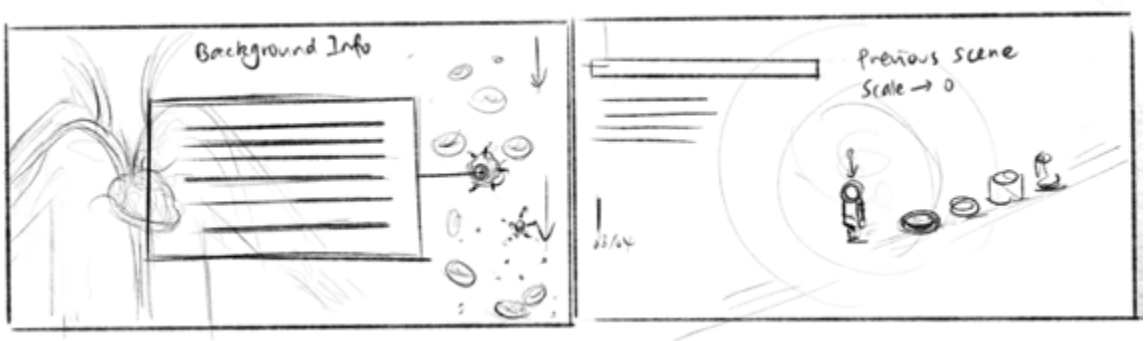
UNFINISHED AGENDA

(The story is to be continued ...)

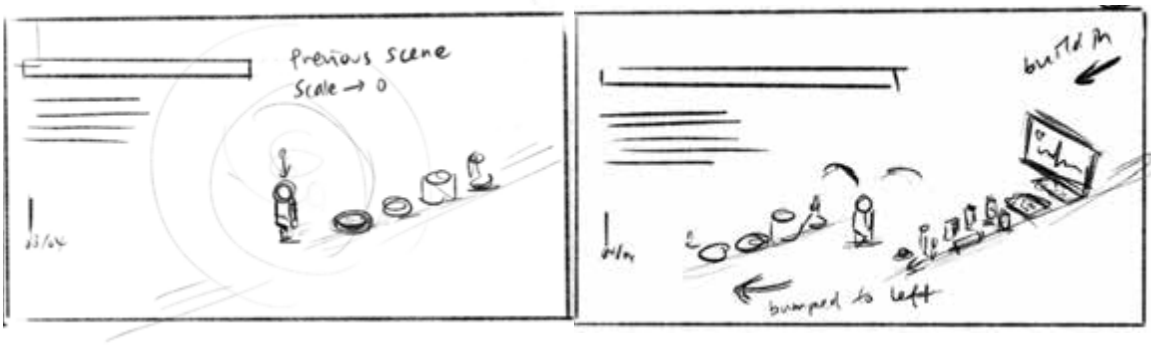
Appendix C | Storyboards



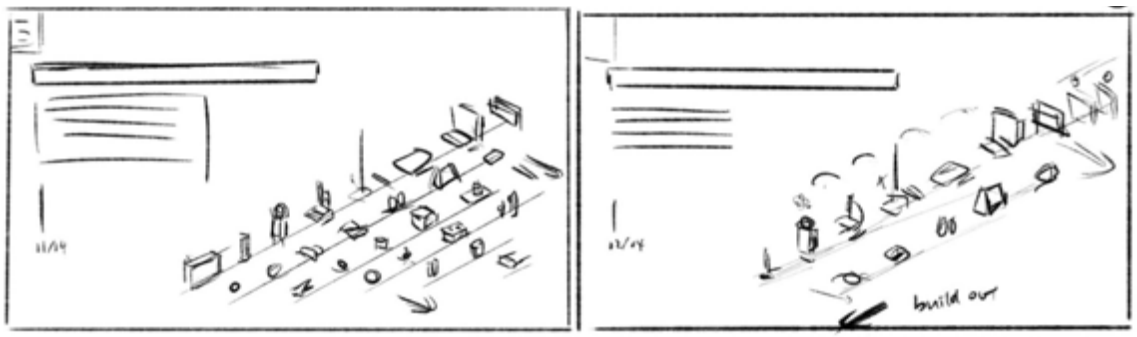
<Motion Design 1-2 > Loading page is composed of a moving amoeba at the center and a progress percentage underneath. The landing page shows a loop animation at the center of the screen, showing Bunsen Burner, petri dishes, and a flask (items that viewers are familiar with and can relate to basic research) A question "How does fundamental research help you?" will be typed on the screen (motion graphics). "Fundamental Research" and "YOU" will be highlighted to build the connection with viewers. The animated icon "Scroll to explore" shows up at this point to provide instruction. Not all text included in the image is intended to be read.



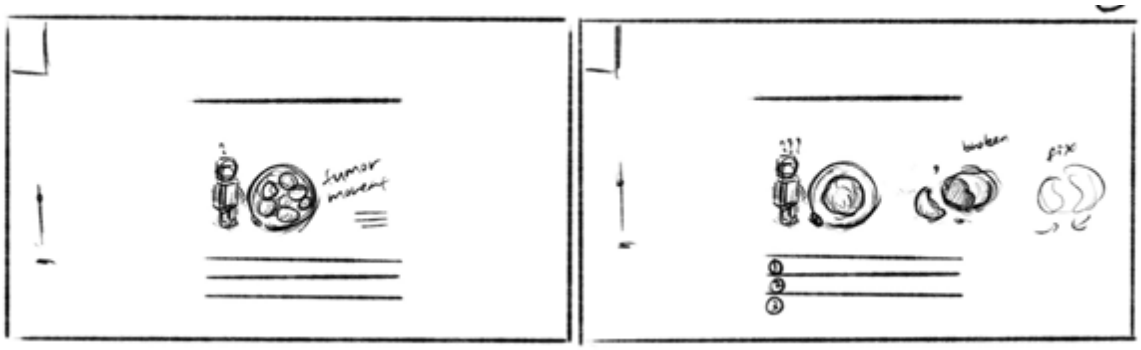
<Motion Design 3-4 > Main page is reached by scrolling. Background animation shows human circulation system, red blood cells and foreign pathogens to represent current health problems. As viewers scrolls and finish reading the paragraph, scene 1 scales down to zero and drops "into" the researcher's head. Scene 2 is composed of a researcher, a flask, and petri dishes with bacteria colonies, slime mold and amoebazoan cells. Models are placed along the isometric grids. Text shows up at the top left corner. Now the researcher has guided viewers to"venture into the world of fundamental research. Not all text included in the image is intended to be read.



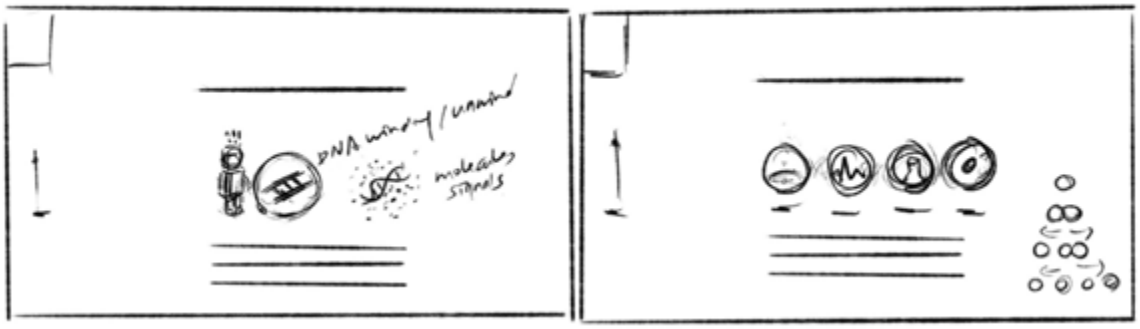
<Motion Design 5> Then a set of models representing "medical and technological" breakthrough enters the screen and bumps the "lab items" to the left. The researcher stays at the same position. Animated arcs indicate the relationship between research and medicine. This is the end of the introduction part 1, which generally states the fact that we depend on fundamental research to face health challenges. As viewers scroll, the scroll bar shows the progress. Not all text included in the image is intended to be read.



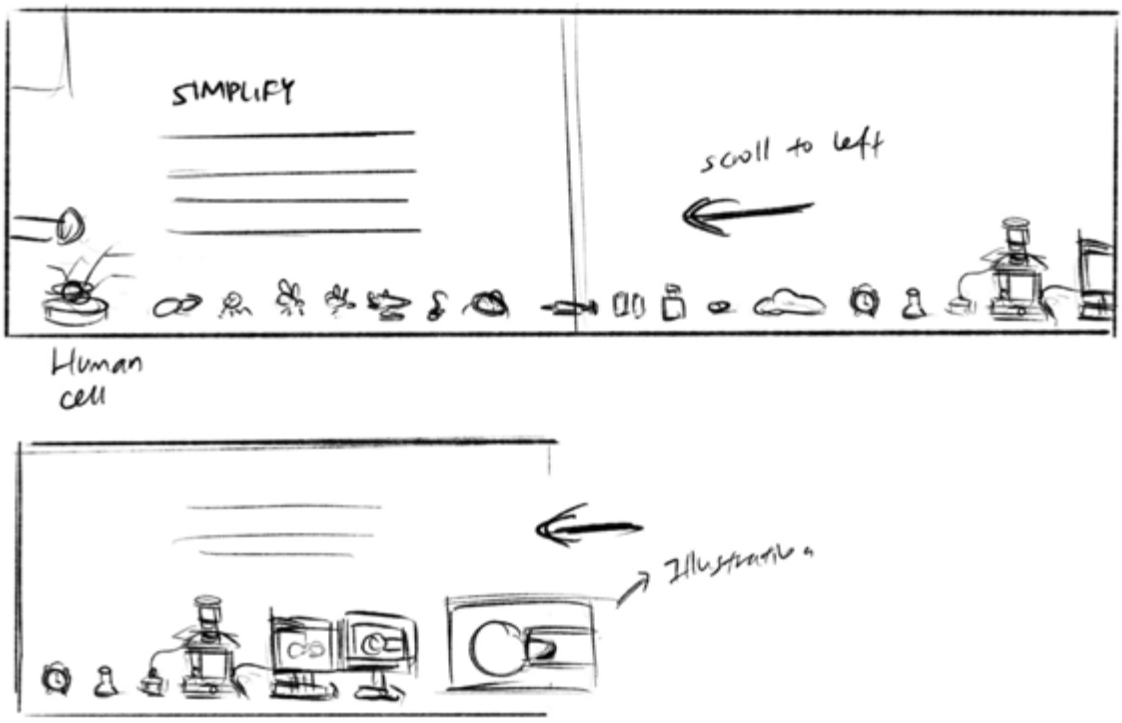
<Motion Design 6-7 > Page number changes to 02. Previous models build out along the isometric axis. The researcher stays. A new set of models build in along the same axis, displaying a broader set of items involved in basic sciences while introducing "what is fundamental research?". Models to be reused in the next scene are positioned at the center. The rest of the models leave the screen along the isometric axis, meanwhile slightly enlarging the models stay on the screen. Animated arcs indicate the research process. This is the end of the introduction part 2. Not all text included in the image is intended to be read.



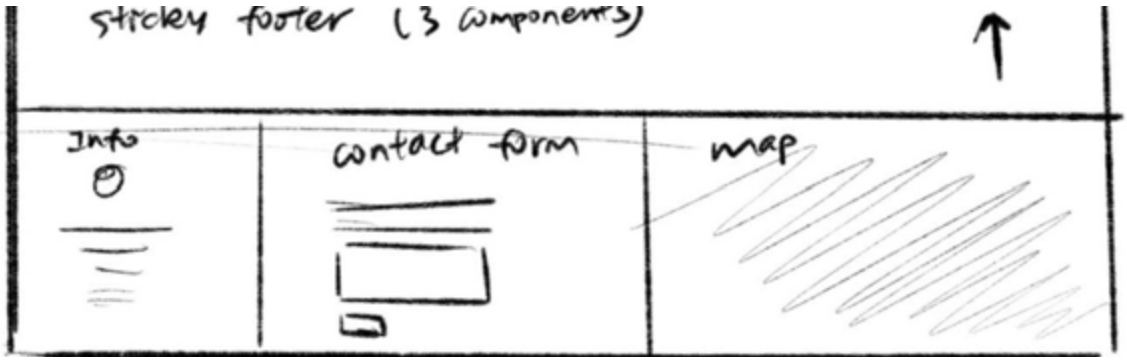
<Motion Design 8 > Introduction section 2 are scrolled up immediately followed by section 3. Researcher and one capsule show up at the center of the screen. A circle appears in the motion of "trim path" behind the capsule where the animation of "cancer cell movement" are shown. Three question mark appears on top of the researcher's head, indicating that "before we can cure diseases, researchers need to find answers to many questions", and that the all of these basic questions fall into three categories. Scrolling controls the highlighting of each question as well as the progress of the animations that represent the question. The animations are masked by the circle. Not all text included in the image is intended to be read.



<Motion Design 9> The same pattern is used for the last page of this section. As the new section "Strategy" is introduced to the screen. The circle with animation playing inside split into 2, 3 and 4, representing "Simplify", "Test", "Predict", and "Screen", with the effect of "simple choker" and " fast blur" in AE. This is the last scene of the Introduction page. Users can click into each title to read more. Not all text included in the image is intended to be read.



<Motion Design 10> Long horizontal scrolling page is designed for the content page. The body paragraph is presented at the center with the 3D models and images show up at the lower 1/3 of the screen. As users scroll, the imagery move horizontally. Text transitions are achieved by the change of opacity. Not all text included in the image is intended to be read.



<Motion Design 11> Scrolling up the main page reveals the stick footer. T**he** footer is composed of contact information, contact form and a map. Not all text included in the image is intended to be read.

Appendix D: HTML (JavaScripts Incorporated)

```
<html>
<head>

    <title> How Does Fundamental Research Help You </title>

    <link href="FundamentalResearchHelpYou.css" rel="stylesheet" type="text/css" />

   <script src="particle_sdl.js"></script> // optional HTML canvas animation

</head>
 <body>

 <div id="Arena">

        <div id="Container">

            <img id="preface" src="opening.gif"></img> // opening animation

            <video id="Content" loop>

            <source type="video/webm;" src="animatics_whole.webm"></source>

            <source type="video/mp4;" src="animatics_whole.mp4"></source>

            <source type="video/ogg;" src="animatics_whole.ogv"></source>

            <p>Sorry, your browser does not support the &lt;video&gt; element.</p>

            </video>
        </div>

        <audio id="ArenaAudio" src="bg_music.mp3" loop></audio>

        <canvas id="ArenaCanvas"> </canvas>

        <div id="ContactForm">

            <form method="post" action="server.php">

            <p><label>name: <input name="username" type="text" placeholder="please input
 name"></label></P>

            <p><label>e-mail: <input name="mailaddr" type="text"></label></P>

            <p><label>message: <input name="message" type="text"></label></P>

            <p><button>send me</button></p>

            </form>

          </div>
```

```
<div id="Afterword"> // sticky footer
        <div id="awContact">
            <div id="awContactImg1"> // contact info
                <img id="AfterwordImg1" src="mtxx20180308_1.png"></img>
            </div>
            <div id="awContactImg2">
                <img id="AfterwordImg2" src="mtxx20180308_2.png"></img>
            </div>

            <div id="awContactForm"> // Contact form
                <p class="awTitle">CONTACT ME</p>
                <ul class="email">
                <li><input type="text" name="name" placeholder="Name"></li>
                <li><input type="text" name="email" placeholder="Email Address"></li>
                <li><input type="text" name="number" placeholder="Phone Number"></li>
                <li class="message"><textarea name="message" placeholder="Message"></textarea>
</li>
                 <button class="btn-define">Submit</button>
                 <a href="mailto" id="send"></a>
                 </ul>
                </p>
              </div>

              <div id="awContactImg2"> // map
                <img id="AfterwordImg3" src="mtxx20180308_3.png"></img>
              </div>
          </div>
</div>
```

```
<script type="text/JavaScript">

 // get HTML ID

 var arenaDiv = document.getElementById("Arena");

 var prefaceImg = document.getElementById("preface");

 var ContentVideo = document.getElementById("Content");

 var arenaAudio = document.getElementById("ArenaAudio");

 var arenaCanvas = document.getElementById("ArenaCanvas");

 var contactForm = document.getElementById("ContactForm");

// Hide video and footer information

ContentVideo.style.visibility = "hidden";

contactForm.style.visibility = "hidden";

 // Variation Initialization

 var arenaScale = 500; // how much to play when scrolling once

 var videoTimerID = 0;  // videoPlay timer

 var canvasTimerID = 0; // background animation Timer

 var part = CreateParticle (3, "ArenaCanvas"); // background animation, support 3 styles


//load document, main event handler function

 document.onreadystatechange = function() {


//once the video/document finishes loading, get video duration, set scrolling depth;

    if(document.readyState == "complete") {

    totalDuration = ContentVideo.duration;

     arenaDiv.style.height = Math.floor(totalDuration) * arenaScale + "px"; // set unit to "px"
```

```
    //set canvas timer for background animation, loop every 40 seconds;
     canvasTimerID = window.setInterval(function(){part.drawDots();}, 40);
   //play background music
   arenaAudio.play();
  }
// get document height
function getDocumentTop() {
      var scrollTop = 0, bodyScrollTop = 0, documentScrollTop = 0; // different browsers
      if(document.body) {
            bodyScrollTop = document.body.scrollTop;
            }
      if(document.documentElement) {
            documentScrollTop = document.documentElement.scrollTop;
            }
      // console.log("==="+bodyScrollTop+"|"+documentScrollTop);
      scrollTop = (bodyScrollTop - documentScrollTop > 0) ? bodyScrollTop :  documentScrollTop;
      return scrollTop; // return the bigger value
}
// get window height
   function getWindowHeight() {
         var windowHeight = 0;
         if(document.compatMode == "CSS1Compat") {
               windowHeight = document.documentElement.clientHeight;
         } else {
               windowHeight = document.body.clientHeight;
               }
         return windowHeight;
      }
```

```
// get scroll bar height
function getScrollHeight() {
    var scrollHeight = 0, bodyScrollHeight = 0, documentScrollHeight = 0;
    if(document.body) {
        bodyScrollHeight = document.body.scrollHeight;
        }
    if(document.documentElement) {
        documentScrollHeight = document.documentElement.scrollHeight;
        }
    scrollHeight = (bodyScrollHeight - documentScrollHeight > 0) ? bodyScrollHeight :
documentScrollHeight;
    return scrollHeight;
}

// Scrolling event-handler
window.onscroll = function() {
  closeTimer();
  var s_Top = getDocumentTop();
  var s_Height = getScrollHeight();
  var w_Height = getWindowHeight();
  if(s_Top == 0) {
    showOnTop();
  } else if(s_Height == s_Top + w_Height) {
    showOnBottom();
  } else {
    showScroll();
}
```

```
// play video when scrolling
    function scrollPlay() {
        ContentVideo.currentTime = window.pageYOffset/arenaScale;
        videoTimerID = window.requestAnimationFrame(scrollPlay); // update calculation
    }
// Scrolling event function1: regular scroll
    function showScroll() {
    if(prefaceImg.style.visibility !== "hidden") prefaceImg.style.visibility = "hidden";
    if(ContentVideo.style.visibility !== "visible") ContentVideo.style.visibility = "visible";
    if(arenaCanvas.style.visibility !== "hidden") arenaCanvas.style.visibility = "hidden";
    if(contactForm.style.visibility !== "hidden") contactForm.style.visibility = "hidden";
    ContentVideo.style.opacity = 1.0;
    ContentVideo.pause();
    arenaAudio.pause();
    scrollPlay();
  }
//Scrolling event function2: go back to the top and autoplay video
    function showOnTop() {
    if(prefaceImg.style.visibility !== "hidden") prefaceImg.style.visibility = "hidden";
    if(ContentVideo.style.visibility !== "visible") ContentVideo.style.visibility = "visible";
    if(arenaCanvas.style.visibility !== "visible") arenaCanvas.style.visibility = "visible";
    if(contactForm.style.visibility !== "hidden") contactForm.style.visibility = "hidden";
    ContentVideo.style.opacity = 1;
    ContentVideo.play();
    arenaAudio.play();
    if(canvasTimerID == 0) {
        canvasTimerID = window.setInterval(function(){part.drawDots();}, 40);
        }
}
```

```
    function showOnBottom() {
        if(prefaceImg.style.visibility !== "hidden") prefaceImg.style.visibility = "hidden";
        if(ContentVideo.style.visibility !== "hidden") ContentVideo.style.visibility = "hidden";
        if(arenaCanvas.style.visibility !== "hidden") arenaCanvas.style.visibility = "hidden";
        if(contactForm.style.visibility !== "visible") contactForm.style.visibility = "visible";
    }


    // close Timer, cancel animation
    function closeTimer() {
        if(canvasTimerID > 0) {
        window.clearInterval(canvasTimerID);
        canvasTimerID = 0;
        };

        if(videoTimerID > 0) {
        window.cancelAnimationFrame(videoTimerID);
        videoTimerID = 0;
        };
     }


};


    </script>
</body>
</html>
```

Appendix E: CSS

```
#Arena {
   display: block;
}

#Container {
   position: fixed;
   left: 0;
   top: 0;
   width: 100%;
   height: 100%;
}

#preface {
   position: fixed;
   left: 0;
   top: 0;
   width: 100%;
   height: 100%;
   opacity: 0.5;
   bject-fit: fill; /*fill | contain | cover | none | scale-down */
}

#Content {
   position: fixed;
   left: 0;
   top: 0;
   width: 100%;
   height: 100%;
   z-index: -100;
   opacity: 1.0;
   object-fit: fill; /*fill | contain | cover | none | scale-down */
}
```

```
#ArenaCanvas {
position: fixed;
min-width: 100%;
min-height: 100%;
width: auto;
height: auto;
color: “#555”;
background-color: “#000”;
z-index: 100;
}

#Afterword {
width: 100%;
opacity: 1.0;
}

#awText {
width: 100%;
background-color: #DCDCDC;
z-index: 100;
}

#awContact {
position: fixed;
bottom: 0;
width: 100%;
background-color: #DCDCDC;
z-index: -100;
}

#awContactImg1 {
position: relative;
width: 100%;
}
```

```
#awContactImg1 img {
min-width: 100%;
}

#awContactImg1 button {
position: absolute;
right: 10; top: 10;
z-index: 50;
}

#awContactImg2 {
width: 30%; height: 200px;
float: left;
}

#awContactImg2 img {
object-fit: fill; /*fill | contain | cover | none | scale-down */
}

#awContactForm {
width: 30%; height: 200px;
float: left;
/*display:inline-block;*/
}

#awContactImg3 {
width: 40%; height: 200px;
float: left;
}

#awContactImg3 img {
max-width: 100%; min-width: 100%;
object-fit: fill; /*fill | contain | cover | none | scale-down */
}

p font-family DINPro {
   font-size: 24px;
}
```

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VITA

Tianxing "Mary" Shi was born in Beijing, China. Grew up in a family of researchers, Mary was exposed to science at an early age and showed great interest in chemistry and biology since middle school, which has always been encouraged by her parents.

Mary continued to pursue biology at the University of Hong Kong of Science and Technology. During her time in college, she worked as a research student in the marine natural product lab and as an chief art editor for the student editorial. In the June of 2014, she received an Honored Bachelor of Science in Biology. Upon graduation, Mary continued to work in cellular and molecular field as a full time graduate research fellow in the University of Hong Kong, Li Ka Shing Faculty of Medicine.

Years of reading research papers and design magazines, has largely inspired her creative and critical thinking and made her realize the essential role of visualization in explaining complex information. These experiences peaked her interest in attending the graduate program of Medical and Biological Illustration at Johns Hopkins School of Medicine, Department of Art as Applied to Medicine where she currently attends. The curriculum has challenged her to use her science background, research experience, artistic skills and design sense to clearly express scientific and medical information to a wide variety of audiences.

During her first year of graduate study she was awarded the Association of Medical Illustrators Award of Excellence in the animation category. She is currently a candidate to receive a Master of Arts on May 23, 2018.